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ALAN MONCRIEFF, M.D.

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R. DAVIES-COLLEY, C.M.G., M.Ch.

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The Medical Aspects of Saint-Simon's "Mémoires"

By J. D. Rolleston, M.D.

Louis de Rouvroy, Duc de Saint-Simon, author of the celebrated *Mémoires*, was born at Versailles on January 16, 1675, the son of Claude, Duc de Saint-Simon, a favourite courtier of Louis XIII, and died on March 2, 1755. The *Mémoires* which he began writing at 19 cover the period 1694 to 1723, so that they include twenty-one years of the reign of Louis XIV and eight years of the Regency. In these *Mémoires* Saint-Simon, who has been described as "the greatest painter of the century" (Sainte-Beuve), "the Tacitus of French History" (Dowden) and "the most vivid and graphic painter of contemporary history" (Saintsbury), has incorporated numerous passages of medical interest. According to the Surgeon-General's catalogue (s.v. Saint-Simon) the only previous works on the medical aspects of the *Mémoires* are a paper by Major Rieux, assistant professor at the Val-de-Grâce Military Hospital, entitled "L'observation médicale dans les Mémoires de Saint-Simon" and a Paris thesis by Mlle Suzanne Thizy entitled "Saint-Simon, Clinicien". Probably the chief reason for the neglect of the *Mémoires* by the medical historian is the vast amount of appallingly dull matter in the twenty volumes of the work, so that most readers will be inclined to agree with Macaulay, who on finishing them said: "I am more struck with the goodness of the good parts than ever. To be sure the road from fountain to fountain lies through a very dry desert". (*Life and Letters of Lord Macaulay*, by G. O. Trevelyan, 1889, 558). There is an abbreviated translation by Arkwright in which much of the passages of medical interest is omitted.

The passages in the *Mémoires*[1] of medical interest may be classified under the headings of prevalent diseases, portraits of contemporary doctors and miscellaneous topics.

PREVALENT DISEASES

Acute infections.—Smallpox is by far the most frequent of all the diseases mentioned by Saint-Simon, over fifty cases being noted, a large proportion fatal. The victims included Saint-Simon himself (18, 356 ; 19, 180), his two sons (14, 52), the Queen of Spain (18, 271), and the Duc de Noailles (5, 166) who recovered, and the Emperor Joseph I of Austria (9, 182), the Old Pretender's daughter (10, 180), Saint-Simon's mother and sister (1, 78), and Monseigneur (9, 105) who died. The disease was particularly prevalent in Versailles in 1711 (9, 310, 407) and in Paris in 1717 (14, 167).

Smallpox is no respecter of unvaccinated persons, and the frequency of the disease among royal personages and courtiers in the prevaccination era is a striking proof of the efficacy of Jenner's discovery, as since then the disease has been almost unknown in the upper classes among whom conscientious objectors are rare. As regards the sequelæ of smallpox may be mentioned facial disfigurement in the Queen of Spain (18, 271), Pontchartrain (9, 340), and Sieur de Neufchâtel (10, 57), loss of one or both eyes in Phelypeaux (1, 247), and Normoutiers (2, 383-4 and 5, 26) and dementia in Mme

[1] The volume and page numbers in brackets throughout the text refer to the 1856-58 Edition of the *Mémoires*.

Desmarets (13, 167). The combination of *pourpre* and smallpox in the case of Monseigneur was obviously hæmorrhagic smallpox (9, 153). It is noteworthy that Saint-Simon, in accordance with the doctrine of the "heating regimen" overthrown by Sydenham, attributes the death from smallpox of the Prince d'Epinoy to premature change of linen and fresh air (4, 348).

Although *scarlet fever* was differentiated from the other acute exanthemata and given its present name by Sydenham in 1683, it does not seem to have received general recognition as an independent disease until much later. Fuller, for example, as I have shown elsewhere (1937), who gave such a detailed description of smallpox and measles,

LOUIS, DUC DE SAINT-SIMON.

[Reproduced from the *Mémoires complets et authentiques*, Vol. I, 1856].

gave little account of scarlet fever in his *Exanthematologia* published in 1730. It is therefore not surprising to find no mention of scarlet fever under that name in the *Mémoires*, though the mysterious disease named *pourpre* which carried off the son of the Maréchal de Boufflers (9, 84), and M. Seignelay (10, 163), may have been an example of the kind.

Several cases of *measles* are mentioned, the sufferers being an English prince and princess (6, 194), Mme de Saint-Simon (10, 234 and 11, 81), the *fils de France* (10, 126), and the Princess of Modena (17, 411). In 1720 there was an outbreak of measles in Paris (17, 424).

Erysipelas.—This disease is mentioned only once, but the circumstances are of special interest (19, 142-5). The recently married Princess of Asturias, the Regent's daughter, developed erysipelas of the face complicated by cervical adenitis. This phenomenon alarmed her parents who thought it might be some kind of venereal lesion transmitted by her father who was a notorious debauchee. Saint-Simon was consulted and was able to reassure them that the adenitis was merely due to erysipelas. Guinard accordingly

has pointed out that the first description of cervical adenitis as a complication of erysipelas usually attributed to Chomel is really due to Saint-Simon.

Puerperal mortality.—Seven cases of deaths in child-bed among the court ladies are mentioned (**2**, 359 ; **10**, 365 ; **11**, 98 ; **11**, 435 ; **14**, 287 ; **17**, 144 and **19**, 449). With the exception of the Duchesse de Mélun (**14**, 287), whose death was due to post-partum hæmorrhage attributed by Saint-Simon to her refusal to be bled in pregnancy, there is nothing to indicate whether the deaths in the other cases were due to infection or not.

Malaria was remarkably prevalent at Versailles and Marly owing to the marshes in these districts. We know from the *Journal de la Santé du Roi* (Le Roi) that Louis XIV was attacked. On two occasions Saint-Simon himself developed tertian fever, once in 1707 (**6**, 104) when he was at Forges, and later in 1719 (**17**, 257) when Mme Saint-Simon also had a malignant fever with which she was extremely ill for six weeks (**17**, 235).

As in the case of mercury for syphilis, cinchona was occasionally used in excess as we learn from the case of M. de Beauvilliers, who Saint-Simon says was killing himself with cinchona to arrest an obstinate fever accompanied by a troublesome diarrhœa (**3**, 43), a condition which may well have been *typhoid fever*. From lack of detail it is of course impossible to determine what was the nature of the fever which was the cause of death of the Dauphine (**10**, 79), M. de Soubise (**10**, 221) and Fénelon (**11**, 437). For the same reason it cannot be said whether the form of low fever mentioned by Saint-Simon as occurring in Flanders among the troops during the campaigns of Louis XIV was trench fever, as suggested by Strong, or not.

Plague.—Several references are made to the great epidemic of plague which occurred at Marseilles in 1720, spread over a large part of Provence, and did not come to an end until 1722 (**2**, 29 ; **7**, 70 ; **18**, 46). In 1723 when the epidemic had quite died out Saint-Simon relates that the barriers were removed, commerce was re-established with all foreign countries and thanksgivings were offered in all the churches of the kingdom (**19**, 439).

Chronic diseases.—Among chronic infections mentioned by Saint-Simon syphilis under the name of *vérole* undoubtedly holds the first place. As I have discussed this subject at some length in the *British Journal of Dermatology and Syphilis* (1941), I will deal with the matter here very briefly. Particularly severe attacks of bone syphilis occurred in the cases of the Duc de Vendôme (**2**, 65, 419 ; **3**, 67 ; **5**, 133) and his brother the Grand Prior (**5**, 140). Both the Duke and another eminent soldier, M. de Vaudemont (**6**, 11), underwent the "grand remedy" which produced abundant salivation owing to the large amount of mercury employed. Several other examples of syphilis among the courtiers are mentioned in the *Mémoires*, including cases of noble ladies infected by their husbands.

As regards Louis XIV, though he was doubtless often exposed to infection owing to his promiscuous behaviour in the early days of his reign, when, as we learn from the *Journal de la Santé du Roi*, he undoubtedly contracted gonorrhœa, there is no evidence in the *Mémoires* or elsewhere that he acquired syphilis.

Cardinal Dubois, one of the most profligate men of a licentious age, and the subject of genito-urinary disease for which he was operated on by the famous surgeon La Peyronie, was probably also another subject of gonorrhœal infection (**20**, 5).

Tuberculosis.—Many cases of lung disease probably of a tuberculous nature find mention in the *Mémoires*, of which the following are examples: The Duchesse de Berwick died of "Consomption" at Montpellier, where her husband had taken her for a change of air (**2**, 84).

The Duc de Caderousse who had long been very ill with his chest made a perfect recovery under treatment by Caretti, a well-known quack (**2**, 136), while Père Valois, a celebrated Jesuit (**2**, 425), and the Marquis de Saint-Simon, the oldest member of the writer's family (**10**, 222 and **15**, 302), both died of a "chest disease" (**2**, 425), and "phthisie" carried off a Spanish nobleman named Duc de Liria (**18**, 384). The most remarkable case was that of Mme de Clerambault of whom the following description suggests a combination of pulmonary and laryngeal tuberculosis: "When young she almost died of a chest disease and was strong minded enough to pass a whole year without uttering a word" (**3**, 384 ; **19**, 427). It may not be generally known that an Honorary Fellow of this Society and a former President of this Section when suffering from laryngeal tuberculosis also adopted this silent regimen and made a complete recovery.

As regards the extrapulmonary localization of tuberculosis, it is remarkable how many of Saint-Simon's personages, of whom the most notable example was Guy Crescent Fagon,

Louis XIV's physician (3, 337), were described as hunchbacks (*bossus*), though of course it is impossible to say whether the spinal deformity in every case was due to tuberculosis.

An example of "King's Evil" is afforded by Mme de Soubise and several of her children who were all "touched" by Louis XIV but without success (7, 60). Another instance of the "King's Evil" was that of the Queen of Spain. It did not, however, prevent her uxorious husband from sleeping with her until a few days before her death (19, 66).

Leprosy.—This disease is mentioned once, the patient in question being M. de Lavardin, lieutenant general of Brittany, who is said to have inherited the disease from the Rostaing family to which his mother belonged (3, 209).

Gout.—As might well be expected owing to their indulgence in highly nitrogenous diet, large consumption of alcohol and lack of exercise, a great number of the courtiers were victims of gout. Among the most eminent of about forty sufferers mentioned by Saint-Simon were Louis XIV himself who had numerous protracted attacks (1, 10; 4, 437; 5, 19; 8, 59; 12, 312; 13, 98; 19, 442), Saint-Simon's father (1, 47), the Prince de Conti (7, 41), M. de Boufflers (7, 362), and the Duc de Vendôme (8, 421).

Cancer.—About half a dozen cases of cancer are mentioned in the *Mémoires* (1, 319, 416; 10, 186; 13, 136; 14, 51; 20, 65), all but one of which were in women. In only three cases, however, was the site mentioned, the breast being affected in two and the mouth in one. In one of them (Mme de Vieuville) it is stated that she kept the cancer secret until two days before death, and only her maid knew about it and dressed it (13, 136), while in the other (Mme Bouchu) the breast was amputated and the patient did not die until many years later of pneumonia (10, 186). The only case of cancer in a man was that of the Duc de Lauzun, in whom the mouth was the seat of the lesion (20, 63).

Nervous Diseases.—About forty cases of apoplexy are mentioned, the most notable subjects being La Bruyère (1, 323), the Duchesse de Bouillon (11, 104), and the Duke of Marlborough (19, 325), of whom Saint-Simon relates that for more than three years before his death an apoplexy had so weakened him that he wept almost incessantly and was no longer capable of anything. Of James II Saint-Simon states that he developed paralysis of part of the body without the head being affected (3, 85).

Other evidence of instability of the nervous system mentioned by Saint-Simon is the occurrence of tics, examples of which were noted in Mme de Nemours (6, 60) tic of the shoulder, Duchesse de Chatillon (6, 299) facial tic, Peter the Great (14, 427) facial tic, and Don Michel Guerra (19, 36), whose case is vividly described as follows: "In spite of good health he showed a strange ailment; his head turned convulsively to the left side. Usually this was slight but almost continuous with little jerks. He was already in this state when he visited Paris on his return from Milan to Spain. Afterwards it increased and its violence was sometimes so great that his chin passed over his shoulder for a few moments, several times in succession. I saw him at home, his elbow on his table, holding his head with his hand to keep it still, or in bed, so as to control it better. He spoke to me about it freely, and it did not prevent conversation. He had tried several remedies in Italy and Spain without success and had sought advice in Madrid. He did not get any considerable or long-standing relief except in the baths at Barèges, and he was on the point of returning there when I left Spain."

Mental diseases.—In a medico-psychological survey of the court society in the time of Louis XIV Dr. Cullère, a distinguished French alienist, remarks that the *Mémoires* of Saint-Simon as well as the letters of Mme de Sevigné furnish us with examples of extremely interesting forms of mental disease. He quotes as an example of toxi-infective psychosis the case of the Marquis de Maulevrier, Colbert's nephew, who committed suicide by throwing himself out of a window during a maniacal attack in the course of pulmonary and laryngeal tuberculosis (5, 153). Another instance of the kind was that of Mme Desmarets (13, 167-8), who became demented after an attack of smallpox.

Other cases of psychosis in the *Mémoires* are those of M. de Tracy, who developed a traumatic psychosis following a wound in Flanders and died in the asylum of Charenton some years later (4, 346). The Duchesse de Charoste appears to have been a borderland case. This lady died at the age of 51 after more than ten years' illness without being able to be moved from her bed, see any light, hear the slightest sound, utter more than two words consecutively or change her linen more than two or three times a year, and always demanding extreme unction after such an effort (10, 282).

The mysterious condition known as "vapours", which according to Saint-Simon was first described by the Abbé Testu (5, 194), appears to have been a sort of neurasthenia.

It is mentioned as occurring in seven other persons beside the Abbé, all but one of whom were men, viz. Chamillart (5, 358), Pontchartrain (6, 294), Louis XIV (13, 93), the King of Spain (14, 67, 244), the Duc de Noailles (15, 48), Mme de Chevry (17, 467), and the Duc de Veragua (18, 409).

Alcoholism.—I have dealt at some length elsewhere (1940) with the prevalence of alcoholism among the members of the court of Louis XIV and the Regent which can be explained if not excused by the terrible monotony of their life. Cannan remarks that "there was nothing to do at Versailles except to contemplate the king's majestic person from morning to night". The most notorious example of collective alcoholism at this time was furnished by the suppers of the Duke of Orleans which were attended by persons whom he called his *roués* (13, 357). These consisted of his mistresses, and other society ladies of easy virtue, army officers and others whose pleasure lay in deep drinking, blasphemy and licentious talk. The scandal provoked by these suppers induced Saint-Simon on several occasions to remonstrate with the Regent (12, 58-9; 13, 359; 14, 279), who made a promise to reform which he never fulfilled. Mme de Vendôme was an example of familial alcoholism, as her husband, the celebrated general, in addition to being syphilitic was a man of intemperate habits, and her brother-in-law, the Grand Prior, another syphilitic subject, for forty years never went to bed without being carried there dead drunk by his lackeys (12, 106). Mme de Vendôme died at the early age of 41 "worn out by strong drink of which she had a cabinet full" (15, 322). Louis XIV himself, though an enormous eater (12, 314, 384), appears to have been only a moderate drinker (12, 513). In case Saint-Simon's picture of alcoholism should be discredited on the ground of his being anything but an impartial witness, as he himself admits (20, 91), confirmatory evidence, as Le Breton points out, of the prevalence of alcoholism among the courtiers is offered by contemporary writers, particularly La Bruyère, Bussy-Rabutin, Courtils de Sandras and Duclos.

Surgical diseases and operations.—Stone in the bladder. Of thirteen operations mentioned in the *Mémoires* five were for this condition. The first was performed on Fagon, the King's physician, by Mareschal who removed a very large stone (3, 337). The second case was the Maréchal de Lorges, Saint-Simon's father-in-law. He was operated on by the itinerant lithotomist Frère Jacques, who refused any other help or advice but that of Milet, a surgeon major in De Lorges' bodyguard. Death took place three days after the operation (4, 34-5). The third case was that of the Comte d'Avaux, French Ambassador to Holland, who also died, at the age of 74, after a second operation for stone by an unnamed surgeon (7, 79). The fourth case was that of the Comte de Toulouse who was successfully operated on by Mareschal, and made an uninterrupted recovery. Mareschal received 10,000 crowns as a fee which he reluctantly accepted by the King's orders (10, 17). The fifth was Dangeau, the author of the well-known *Mémoires,* who in addition to operation for fistula in ano underwent two lithotomies (18, 64). On none of these occasions is the name of the surgeon given. An operation for an abscess of the bladder, probably of gonorrhœal origin, was performed in the course of five minutes on Cardinal Dubois by La Peyronie, the king's chief Surgeon, in the presence of Mareschal, Chirac and other celebrated physicians and surgeons. Death took place twenty-four hours later (20, 5). Mention is made of four cases of operation for fistula in ano which became as fashionable a complaint after the operation for this condition on Louis XIV as appendicitis did more than two centuries later in the case of Edward VII. The first operation was performed by Mareschal on Courcillon, a man of depraved tastes which were popularly regarded as the cause of the condition (5, 271). He subsequently underwent re-amputation of the thigh for a wound received at Malplaquet (8, 115). The second case was that of Dangeau (*v. supra*). The third operation for fistula in ano was performed on a lady, Mme de Saint-Géran, with successful results (7, 436). The fourth was performed on the Cardinal de Mailly (18, 193). Recovery was uneventful for five months apart from a slight discharge which suddenly stopped, the heart became affected, and he died ten to twelve hours later.

Of the three remaining successful operations, one was performed by Mareschal, which consisted in free incision of Saint-Simon's arm for cellulitis following phlebotomy carried out by Drain, one of the court surgeons (4, 254-5), and another was a radical cure of double inguinal hernia in the Maréchal de Villeroy by an unnamed surgeon (2, 221). In the case of an amputation of the breast for cancer in Mme Bouchu, who made a good recovery and died many years later of pneumonia, the name of the surgeon is also not given (10, 186). In this connexion reference may be made to the case of the Duchesse de Sully who "had an abscess in a place which her modesty would not allow

her to show to a surgeon. Her maid dressed it for some time and explained the case to a surgeon waiting behind the door. She did what he prescribed, but the method of treatment soon brought her to her grave" (18, 130).

Finally the *Mémoires* contain brief indications of three diseases long before they were described in scientific medicine. These references are all the more interesting as, so far as I have been able to ascertain, they have not received any mention in the historical account of the diseases in question. The first of these, which seems to be a description of achondroplasia, was that of the Abbé de Baudrun who presented the following appearance: "Being an absolute dwarf and extremely lame he joined the Church. In spite of his twisted legs and enormous head he was nevertheless very enterprising with women for winning whose favours he possessed great talents" (2, 413; 9, 26). This Abbé thus closely resembles the patient named "Anatol" described by Pierre Marie who emphasizes the erotic tendencies of achondroplasics. The next case, which seems to be one of spondylitis deformans, is that of Joyeux, Monseigneur's chief valet and Governor of Meudon, of whom Saint-Simon's description is as follows: "His back remained flat, but it seemed to be broken down below where it stuck out and Joyeux walked as if he was folded in two" (5, 148).

Lastly the case of the Comte de Beuvron, "who died very young, losing his blood by the pores of his skin, a disease about which very little is known by doctors", was obviously an example of hæmophilia which, according to Bulloch and Fildes was "entirely undescribed as a distinct morbid entity before the beginning of the nineteenth century" (14, 50).

SAINT-SIMON AND THE MEDICAL PROFESSION

Saint-Simon, like many other eminent laymen before and since his time, does not appear to have had any liking for doctors as a class, as is shown by the frequency with which he declared that they did not understand the nature of the disease which they were treating, as in the cases of the Comte d'Auvergne (6, 130), Maréchal d'Huxelles (8, 102), Sézanne (11, 233), the Duchesse d'Orléans (12, 61), M. de Maisons (12, 301), and the King of Spain (16, 77). On more than one occasion he relates that a quack had been successful, if only temporarily, where the Faculty had failed, as in the cases of Maréchal de Boufflers (9, 424), Louis XIV (12, 377), and Mme de Berri (17, 228). Du Chesne, Fagon's successor as physician to the king's children, receives special praise for not being boastful like most doctors (5, 361), while of Helvétius, Boudin's successor as ordinary physician to the king, he states that he never indulged in gossip like most doctors (7, 115). On the other hand he is unsparing in his eulogy of individual doctors, particularly Fagon (1, 110), physician to Louis XIV, Mareschal his surgeon (4, 121-2) and Hyghens the King of Spain's physician (19, 14-15). D'Aquin, Fagon's predecessor is described as a great courtier, but as avaricious, crafty and over-reaching (1, 109). In the case of Chirac, physician to the Regent and afterwards to Louis XV, an acknowledgment of his medical competence is more than counterbalanced by a condemnation of his irreligion and audacity (11, 437; 13, 258; 15, 320). The following appreciations of Fagon and Mareschal, Louis XIV's most eminent physician and surgeon respectively, deserve to be quoted in full: "Fagon was one of the finest and best minds in Europe, interested in everything related to his profession, a great botanist, a good chemist, a clever surgeon, an excellent physician, a great practitioner. His knowledge was extensive, no one was a better physicist than he; he had a good understanding of the different departments of mathematics. He was quite disinterested. He was a keen friend but a relentless foe. He loved virtue, honour, valour, science, industry and merit, and always tried to support them without any other reason. He was the most implacable enemy of those he called charlatans, that is, persons who pretended to have secret remedies, and his prejudices carried him too far in this respect. He loved his Faculty of Montpellier and worshipped medicine. In his opinion it was not permissible to treat any one except by a recognized medical method sanctioned by the Faculties whose laws and orders he regarded as sacred. At the same time he was a subtle courtier and had a perfect knowledge of the king, Mme de Maintenon, the court and society. He had been the doctor of the king's children since Mme de Maintenon had been Louis XIV's housekeeper, and that was how he had been connected with her. The favour and consideration shown him, which were extreme, never let him forget his place" (1, 110-11). Many years later, however, when Fagon was in poor health and showed a remarkable physical and mental decline, Saint-Simon on quite inadequate grounds, as Le Roi has shown, accused him of being responsible for the premature death of the king (12, 312).

Fagon's international reputation led William III to consult him twice. On the first occasion the English king disguised himself as a *curé* and was sent away abruptly with the advice to prepare for an early death. On the next occasion, when William consulted him without disguise, Fagon recognized him, and though he did not express a different opinion, was more considerate and prescribed a treatment likely to prolong his life if not to cure the disease (3, 396). On his retirement Fagon took a house belonging to the Jardin du Roi where he devoted his time to the study of rare and medicinal plants, literature and medicine. "He died", says Saint-Simon, "in a very pious manner and at a great age for so deformed and cacochymatous a man" (15, 299-300).

The sketch of Mareschal, with whom Saint-Simon was on very intimate terms, is almost equally eulogistic with that of Fagon (4, 121-2). "He surpassed all in reputation and skill. Besides his professional capacity he was a man who with very little wit had much common sense, was full of honour, probity and aversion for the opposite, straightforward, frank, true and very free in showing that he was so, a good and thoroughly honest man and very serviceable."

High praise is also given to an Irishman named Hyghens, first physician to the king of Spain and a doctor of several universities including that of Montpellier, who attended Saint-Simon during his attack of smallpox in Spain (18, 357). He is described as being an excellent doctor with a good knowledge of surgery, literature and art as well as of drugs (19, 14-15). A special place is occupied by Helvétius (3, 82-3) "a big Dutchman who owing to his not having taken a degree in medicine was detested by doctors and especially by Fagon. He had long been busy in Paris, curing many persons who had been given up by doctors, especially the poor whom he treated with great charity". He appears to have been particularly successful in his treatment of diarrhœa, dysentery, smallpox and other toxic diseases. He introduced the treatment of dysentery by ipecacuanha which he first employed as a secret remedy, but subsequently sold the secret of its composition to the king.

Another physician of whom Saint-Simon had a good word to say was Dodart who succeeded Poirier as first physician to Louis XV, and was described as "a very honourable, moral and mild mannered man, averse to trickery and intrigue" (15, 319). Mention may also be made of a doctor named Petit, for many years physician to Monseigneur who died in 1702 at a great age and was succeeded by Boudin. "He possessed", says Saint-Simon, "intelligence, knowledge and experience, and was a man of honour, and yet he died without ever having consented to admit the circulation of the blood (4, 21)." Other eminent surgeons mentioned by Saint-Simon besides Mareschal are Felix who had operated on Louis XIV for fistula in ano in 1683, bled Monseigneur for an attack of acute indigestion (3, 138), and set the Duc de Rochefoucauld's arm which he had broken while riding (3, 421), and La Peyronie who operated on Cardinal Dubois for an abscess of the bladder (20, 5). He is described as a great surgeon who proved himself to be a great and clever courtier and gained much reputation in the court and in society (17, 143). Lastly mention should be made of Boulduc, the king's apothecary, who like his father had always been much attached to Saint-Simon himself. Saint-Simon declared that he knew at least as much as the best doctors as well as being a man of honour, discretion and good sense (10, 95). It is probable that Saint-Simon was indebted to him as to Mareschal for much information on medical matters.

Numerous unqualified practitioners figure in the *Mémoires*. Of these the most notable were Frère Jacques, the lithotomist, and Caretti, an Italian quack, who in spite of the Faculty amassed a considerable fortune. He treated the Duc de Luxembourg for pneumonia, which had been regarded as hopeless by Fagon, by secret remedies which had often succeeded and caused some relief but only for a few moments (1, 232). He was successful, however, in the treatment of a wound of M. de la Feuillade (2, 136), and of the Duc de Caderousse who had long been suffering from a chest disease (8, 415). Both these cases, according to Saint-Simon, had been regarded as hopeless by their doctors. Another successful quack was a man named Garrus, who employed an elixir, the secret of which was bought by Louis XV, in the cases of Maréchal de Villeroy (17, 155) and Mme de Berri (17, 228). Louis XIV was attended on more than one occasion by a quack. One of these was Lavienne who supplied him with aphrodisiacs (1, 275; 2, 74), and the other was a peasant from Provence named Le Brun who came to Versailles during the king's last illness with an elixir which he said cured gangrene. The condition of Louis XIV was then so desperate that, in spite of Fagon's protest, it was tried and was followed by temporary improvement (12, 377-8). In connexion with unqualified practice reference

may be made to an attack of apoplexy of Saint-Simon's father-in-law, Maréchal de Lorges, who was so extremely ill that the doctors despaired of his recovery. Saint-Simon, however, gave him 130 drops of Gouttes d'Angleterre (black drops) in three doses and complete recovery resulted (1, 261-2).

MISCELLANEOUS TOPICS

Longevity.—Le Breton has drawn attention to the large number of octogenarians of both sexes mentioned by Saint-Simon, and cruelly remarks that they must indeed have been robust to have reached an advanced age in spite of the attention of their doctors with their bleedings, purgings and other remedies. I have myself counted 66 persons in the *Mémoires* who were 80 or over at the time of their deaths, 60 being octogenarians, 5 nonagenarians and 1 a centenarian, the Marquis de Mancera, a grandee of Spain, whose peculiarity was that he never ate bread or anything in its place and retained his health and mental faculties until the end (18, 489). The best known of the other long-lived individuals were Saint-Simon himself and Jean Bart, the celebrated seaman (3, 400) aged 80, Père La Chaise, the ecclesiastic (7, 45) aged 85, Princesse des Ursins (19, 424). aged 85, and the Comte de Gramont (5, 333) aged 86. Louis XIV, it may be mentioned, was only three years short of 80 at the time of his death.

Sexology.—The eighteenth century was the age of sexual athletes, the example being set by Louis XIV, whose powers in this respect even at an advanced age made Mme de Maintenon complain to her confessor (Mongrédien). The palm, however, must be given, even if allowance be made for some exaggeration, to the Abbé de Grandpré, whose sexual capacity far exceeded that of Catullus and of whom Saint-Simon gives the following description: "He was a kind of imbecile and behaved just like one. . . . His body, however, was not like his mind, and women had given him the name of *Abbé Quatorze* which had stuck to him and this prodigy had become so notorious that its singularity had become an excuse for mentioning it" (8, 119). In striking contrast with this case were three examples of impotence. The first of them was the Duc de Coislin (8, 164), who nevertheless had an actress as his mistress. The second was that of the Marquis de Gesvres, whose wife brought an action against him for separation (10, 199-200). The bishop's tribunal, before whom the case came, decided that the husband should be examined by surgeons and the wife by matrons. The case lasted for a long time, causing a great deal of amusement except to the couple who nearly died of shame, and was only terminated by the death of the wife. The third case of impotence was that of the Marquis de Santa Crûz (18, 424). He lost the action brought by his wife who was allowed to marry again. Shortly afterwards a girl brought another action against him for being the father of her illegitimate child and gained her case, so that, as Saint-Simon remarks, he was not lucky in his law suits.

The prevalence of homosexuality in the eighteenth century, to which I have drawn attention in my paper on Casanova (1917), especially among the clergy, is illustrated in many passages in Saint-Simon's work. Notable examples were Monsieur, the brother of Louis XIV (1, 18), the Abbé de Soubise (2, 389), the Abbé Servien (3, 341), the Duc de Vendôme (12, 28), and the Cardinal de Bouillon (12, 28). Reference has already been made to Courcillon whose fistula in ano was attributed to this cause. A remarkable example of transvestitism is furnished by the Abbé d'Entragues (17, 376-7). This person while in exile at Caen for debauchery, was visited by Pelletier de Sousy who found him sitting up in bed, doing fancy work, wearing a woman's lace night cap and patches, and a row of ribbons on his night gown. His visitor mistook him at first for an improper woman and was on the point of retiring when the Abbé disclosed his identity.

Spas.—Numerous spas in France, such as Bagnères, Barèges, Bourbon, Forges, Plombières and Pouges, and in other countries, such as Aix-la-Chapelle, Bath, Carlsbad and Schaffhausen are mentioned in the *Mémoires.* Of the French spas Bourbon seems to have had the greatest number of distinguished visitors, including James II and his wife (3, 85), and Mesdames de Maintenon, Saint-Simon and de Montespan (6, 46). Saint-Simon himself went to Forges in the summer of 1707 to try and get rid of a double tertian fever which he says was only suspended by cinchona (6, 104). As regards foreign spas Peter the Great visited Carlsbad (10, 20), and Lauzun (5, 36) Aix-la-Chapelle, while the Comte de Roye (1, 421) passed eighteen years in England and died at Bath in 1690.

Poisoning.—One of the dark sides of the resplendent age of Louis XIV was the

frequency of real or suspected cases of poisoning of which Saint-Simon reports numerous examples, though the nature of the poison is not stated. We know, however, from other sources, e.g. Cabanès and Nass, that arsenic and perchloride of mercury were the drugs usually employed. In the case of Mme de Verrue, the mistress of M. de Savoie, a powerful antidote saved her life and her beauty did not suffer, but troublesome sequels ensued (2, 439) the nature of which is not disclosed. On two occasions snuff was the vehicle in which the poison was administered. One case was that of the Comte d'Aguilar, a grandee of Spain, who was accused of having poisoned the father of the Duc d'Ossone by this means (3, 126). The other was that of the Duc de Noailles who gave a snuff-box containing excellent Spanish snuff to the Dauphine who died after a few days' illness (10, 79). The king's apothecary Boulduc had no hesitation in regarding the case as one of poisoning (10, 95, 135), as he did later the cases of the Duc de Berri (11, 83), the Dauphin (10, 139), and Dauphine (10, 135) (*v. infra*).

Poisoning was not infrequent in the contemporary court of Spain. Thus we learn that Salazar poisoned his wife (19, 29), just as the Duc de Popoli did his (18, 402), so that it was facetiously said in the Spanish court that to have poisoned one's wife was a necessary condition for achieving distinction. Ferdinand of Spain was suspected of having poisoned his son-in-law, Philip the Handsome (3, 229), but as Prescott (*Ferdinand and Isabella*, 1841, 2, 395), remarks, the suspicion was unsupported by a particle of evidence. In another case which also occurred in Spain the Comtesse de Soissons poisoned the queen, the poison being conveyed in milk (3, 291 ; 6, 443). Other cases of suspected poisoning were those by Penautier, the treasurer of Languedoc, who was involved in the Brinvilliers affair and narrowly escaped with his life (9, 418), and the Comte d'Aguilar, accused of having poisoned the Duc de Vendôme (10, 207 ; 18, 446). The death of Madame, Henrietta of England, the first wife of Monsieur, was ascribed without hesitation to poisoning by Saint-Simon who states that no one ever had any doubt about it. Subsequent investigations, notably by Littré, Cabanès and Nass, and Funck-Brentano among others, indicate that her death was due to acute peritonitis from perforation of a peptic ulcer. Even a slight indisposition in an important personage was liable to rouse the suspicion of poisoning, as is shown by the attack of tonsillitis in the young king, Louis XV, when one of the court ladies caused a sensation by declaring that he was poisoned (18, 180-1).

Post-mortem examinations.—In at least seven cases Saint-Simon, not content with living portraits of some of the principal characters in the *Mémoires*, also gives an account, though naturally incomplete, of their post-mortem examination.

(1) *Louis XIV.*—"On opening his body, which was done by Mareschal, his senior surgeon, with the usual attendants and ceremonies, all the parts were found to be complete and healthy and everything in such perfect order that it was thought he might have lived more than a century but for the errors mentioned which put gangrene into his blood. The capacity of the stomach and intestines was at least double that of men of his height, which is very extraordinary and was the cause of his being such a constantly great eater" (12, 384).

(2) *Mansart.*—In the case of Mansart, nephew of the famous architect, who died after an attack of colic of twelve hours' duration, the extraordinary swelling of the body after death and some spots found on opening the body gave rise to a suspicion of poisoning, but no further steps were taken (6, 244-5).

(3) *Mme de Montespan.*—In her case we learn no more than the fact that "this body once so perfect became the prey of the clumsiness and ignorance of the surgeon of Legendre's wife" (6, 47),

(4) *Duc d'Orléans* (père).—A cerebral tumour appears to have been the cause of his death. "One found on opening the body of the Duke a sort of excresence or foreign body in the head which caused his death after it had reached a certain size" (8, 140).

(5) *The Dauphin.*—The autopsy on the Dauphin took place a little more than twenty-four hours after death in the presence of the whole Faculty (10, 123). Fagon, Boudin and some others (10, 139), were firmly convinced that death was due to poisoning, whereas Mareschal, who performed the autopsy, declared that "there were no definite signs of poisoning, that he had seen autopsies presenting the same appearance in which there had never been any suspicion of poisoning, and that the cause of their death as in that of the Dauphin was the corruption of their blood due to a violent fever".

(6) *The Dauphine.*—Mareschal expressed an identical opinion at the autopsy of the Dauphine when Fagon and Boudin were as before in favour of poisoning (**10**, 135).

(7) *Mme de Berri.*—The autopsy on this lady, whose death according to Saint-Simon was due to Chirac's ill-advised administration of a purgative, merely showed the existence of pregnancy and "derangement in her brain" (**17**, 232).

In his will Saint-Simon expresses the desire that after death his body should be left for at least thirty hours without being touched or displaced except to ascertain that he was no longer alive, and then should be opened in two places, viz. at the root of the nose and in the throat or upper part of the chest, in order to discover for the good of the public what was the cause of his nasal obstruction and attacks of suffocation from which he had always suffered (**20**, 98). There is no record, however, to my knowledge, of his wish having been carried out.

Illnesses of Louis XIV.—The *Journal de la Santé du Roi Louis XIV*, published by Le Roi in 1862, contains a detailed account of the king's health from 1647 to 1711 drawn up successively by his principal physicians Vallot, D'Aquin and Fagon. The chief diseases from which he suffered during this period were smallpox (1647), a tumour in the left nipple (1653), gonorrhœa (1655), an illness at Calais which was probably typhoid fever (1658), measles (1663), necrosis of jaw (1685), fistula in ano (1686), and numerous attacks of gout. The detailed account of his stools suggests that he suffered from chronic enteritis which was aggravated by frequent administration of purgatives and his enormous appetite. The illnesses from which the king suffered which are described in the *Mémoires* were a continuation of the attacks of gout, "vapours", diarrhœa, chronic enteritis and senile gangrene of the leg. His dental history is of some interest. He was born with two teeth, which had the effect of lacerating his nurses' nipples, and at an early age suffered from dental caries. Clumsy extraction of a number of teeth gave rise to necrosis of the jaw and accounted for the inadequate chewing of his food and consequent enteritis. The loss of his teeth naturally caused the king considerable discomfort of which he complained one day during dinner to the Cardinal d'Estrées. "Teeth"! replied the tactful ecclesiastic, "who has any nowadays?" a remark which was all the more amusing as the Cardinal still possessed a remarkably fine set, and was much appreciated by the king and those present at the meal (**11**, 267).

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Some Little-known Medical Practitioners in Mediæval Persia

By Cyril Elgood, M.D., F.R.C.P.

The debt which European Medicine owes to the Persian physicians such as Rhazes, Avicenna, and others, is immense. This paper outlines how the first repayments were made. It was not a conscious repayment any more than Rhazes was intending to instruct the barbarous West. The penetration of European physicians of the post-Harveian School into Persia was the result mainly of political fears and pecuniary desires.

Of the many great phenomena of the fourteenth century one of the greatest is the rise of the Ottoman Empire. Osman (1288-1326), after whom in a corrupt form the Ottoman Empire is named, was the first of the Seljuq tribe of further Asia to become an independent sultan. The third of the line, Murad I (1359-1389), obtained by Genoese ships the transport of his men from the coast of Asia to Gallipoli and he established himself in Adrianople. In spite of the opposition of all the sovereigns of Eastern Europe he established his rule there and actually added Bulgaria and Serbia to his sultanate. His son, Bayazid I (1389-1404), nicknamed The Thunderbolt, inflicted further defeats on the European sovereigns and a little later made war on his eastern frontier against Tamarlane who was then ruler of Persia. The commencement of the enmity between the Turks and the Persians is of great significance for my argument.

The greatest of the Turkish sovereigns of this era was Muhammad II (1451-1481) who captured Constantinople and added Mitylene, the Peloponnese, most of the Balkans, and all Anatolia as far as the Euphrates to his dominions. Towards the end of his life he became ambitious of attacking Italy, and actually made a landing at Taranto. But his Moslem soldiers whom he left there were besieged and compelled to surrender.

From now on the power of the Turks became a scourge both to the East and to the West. In the East Selim I (1512-1520) attacked Shah Isma'il Safavi of Persia on the grounds that he was a heretic, defeated him, and annexed Azerbaijan. Next Egypt and Syria fell and the Sultan of Turkey became the Caliph of Islam. Rhodes, Hungary, and the Barbary States fell in 1522.

To this imperialistic drive, this demand for the subjugation of Christendom, there was naturally a reaction all over threatened Europe. The threat being equally to the whole Christian family, all eyes naturally turned to the Bishop of Rome who, so long their spiritual leader, was now called also to be their temporal leader, their political rallying point. Most unfortunately when the Turkish drive began, such leadership was not forthcoming. The bishopric of Rome was split: an Italian Pope in Rome was opposed by a French Pope in Avignon. Spain, the greatest of the Catholic powers, was occupied with her own affairs, ridding herself of the Moors and exploiting the recently discovered America. Yet the Papacy did what it could. As early as 1444 Cardinal Julian Cesarini had been engaged in fighting the Turks and had actually died in battle. Nor did the Papal galleys ever fail to join forces with the Venetian fleet in the Aegean and Adriatic seas.

The objective of the Papal policy during these years was to protect both the temporal power of the Christian princes and the spiritual liberties of all their subjects. Pope after pope saw clearly that both these were threatened by the victorious progress of the Turk. Pope after pope saw that two things were necessary to put an end to this progress: to unite the Christian princes in a fresh crusade against the infidel. This demanded that they should put away their family quarrels, abandon their selfish policies, and become what they professed to be—a large Christian family. And to attack the Turk on both his western and eastern frontier and so compel him to wage war on two fronts. This could only be done by an alliance with the ruler of Persia which in the light of past Turko-Persian relations did not seem a very difficult feat of diplomacy to produce. These two points are found inextricably combined in scores of papal briefs of this period.

Pope Leo X,[1] writing to Sigismund, king of Poland, in 1515 referred to "this especially favourable opportunity offering, as We have been lately advised by letters of the Grand Master of Rhodes that the Sophy, king of Persia, who now for long passed had conceived a hatred against the Tyrant of the Turks, had delegated an envoy to him (i.e. to

[1] Chron. Carm. Per., I, 15.

the Grand Master) to say that the latter should use every endeavour to report to all Christians and to stir them up, both kings and princes, to take arms against this same Turk". The "Sophy" means Shah Isma'il Safavi.

The battle of Lepanto in 1572 was a glorious victory for the papal forces, and Pope Pius V took the opportunity to send a Brief to Shah Tahmasp I Safavi to acquaint him of the fact and at the same time to urge him to complete the discomfiture of the Turks by attacking their rear with all his might. The Shahs were not for their part averse to so doing, but were too wise to commit themselves before they were assured that the attack on the European front would materialize simultaneously.

Twenty years later Shah 'Abbas I (1587-1629), the greatest of the mediæval Persian shahs, being then on the throne, an extensive embassy was despatched to Europe. This time Husayn Ali Beg came accompanied by Sir Anthony Sherley. The story of the embassy and above all the Sherley brothers reads like a novel. To Anthony Sherley the Shah entrusted a letter offering alliance and friendship with the people of Europe. In it occurs his statement that his country would be thrown open to foreigners and so it was due to Shah 'Abbas that the opportunity was given for Western Medicine to be brought to the Persians. "And to give the more credit and weight", he writes, "to his true and genuine intentions the king opens all his country freely to all kinds of Christians, so that they may enter it, stay and remain there, and depart thence in all security and with every safeguard, giving them besides the most ample privileges both in regard to their persons and their property, trade and affairs."

The answer was the organization of the first papal mission to the Court of Ispahan. A priest, Francisco da Costa, and a layman, Diego da Miranda, were selected; but the Shah did not consider that they were of sufficient nobility of birth to hold ambassadorial office. Finally Fr. da Costa having killed an Armenian over the possession of a boy was compelled to flee the country.

Three years later, that is 1607, the first Carmelite Mission arrived. It consisted of three priests, a lay brother, and a Spanish officer. They had no doctor with them, for one of the party fell ill at Qum and had to call in a Persian practitioner, who, he writes, "found me with a very high fever, and very weak from inability to eat or sleep: it appeared to him that there was insufficient time to give me medicine, as we were about to travel".

For just 200 years the Carmelites remained in Persia. Their diplomatic status gradually became less and less prominent, but they seem never to have lost their great influence at Court, and many of them practised Medicine.

Here is the second factor which was indirectly responsible for introducing Western Medicine into Persia. About the time that the Papacy was calling for a new Crusade an event of stupendous importance had occurred: Vasco da Gama in 1497 had sailed round the Cape of Good Hope. The immediate result of this was that within twenty-five years the Portuguese Government had complete control of the trade of the East Indies and that Persia was brought into touch with Europe from another angle.

The reaction in England of this highly successful Portuguese coup was not to set up a rival company and attempt to defeat the Portuguese on their own ground, but to try to solve the difficulty by finding another route into Persia and India which would be altogether free from Portuguese competition. The next few years were filled with the granting of charters by English sovereigns to English mariners for the discovery, as one Charter has it, "of Regions, Dominions, Islands, and Places unknown". These charters and expeditions crystallized out into the Russian or Muscovy Company which began operations in 1555.

During the twenty years from 1561 to 1581 six trading expeditions were despatched to Persia and none of them, from the point of view of the shareholders at any rate, were successful. The defeat of the Spanish Armada in the English Channel in 1588 put new hope in the hearts of the English merchants, for it showed that the Portuguese, who had become united to Spain under Philip II ten years earlier, were not invincible. A private trading venture to the East was organized by some London merchants in 1591, but resulted in failure. Again their hopes were raised when they heard that a Dutchman had repeated the Portuguese feat of sailing round the Cape to India. On December 31, 1600, the East India Company was duly incorporated under the style of the Old or London Company.

In 1609 the Company's agents were found for the first time in Persia. They reported[2]

[2] Curzon. Persia, vol. ii, p. 546.

that "at Hispahan might be planted a profitable trade if our ships with safetie might lade in the Persian Gulfe; where fifty in the hundred may bee gained from Ormus to Hispaan, and that in eighty dayes travell". A few years later Shah 'Abbas the Great, probably at the request of Sir Richard Sherley, issued a royal edict that "all governors of seaports in Persia shall kindly entertain English shipping". In 1616 the Factors were permanently established at Jask and in 1617 at Ispahan.

Here they found living a Scottish adventurer named George Strachan, who was practising Medicine. The English Company engaged him at a salary of twelve tomans a year, in modern currency about £3 p.a. He was given the rank of Linguist and Surgeon to the Company.

His biography is curious. In 1602 he was in Rome where he entered the Scots College, but apparently never reached even Minor Orders. A desire to travel took him a few years later to Constantinople. From there he passed on to Syria, the Lebanon, and Aleppo. At this last place, having heard that the Amir of 'Anayza was in need of a physician, and with the idea of perfecting his Arabic, he took service with him, although he was then entirely ignorant of Medicine. However, he furnished himself with some prescriptions from a Flemish doctor, bought a book or two, and started to practise. He was enormously successful and only with difficulty some three years later did he escape from his patron, whose sister he had married.

Life as a respectable English official was too dull for him. He was accused of peculation and even of murder, and in August of 1620 he was dismissed from the Company's service.

> "And Strachan our Antechristian Phesitian, for his fflattering, lying, dissimulation, inconscionable stores of purloynment, with his tentarhookes of deere penniworthes of plaisters and purges, sowing dissention in the ffactory, his scandalous reports of poyzoning the Company's servants as the late Agent and William Rhyns, his discouering all the passages of our busines to the ffryers in Espahan through his confession and disloyall service to the Company, intercepting of their letters. How can he be otherwise, being marryed to a More in Arabia, from whom he tooke his runnagate raunge, leaving wyfe and family to prosecute the divells commission in doing evill; continewally despizeth his owne country, and yts church, And confesseth to haue the dispensation of the Pope to dissemble his Religion in all his Pilgrymage. Whose plague infection to remove from our ffactory (by irresistible reasons to the Agent besides costeth the company 100 l. per annum) hath wrought him to act the devill, to make a compleate nomber of my cappitall Aduersaries."[3]

Thus wrote Robert Jefferis, a factor of the Company at Ispahan. The authorities at Surat, however, seem to have taken the side of Strachan, and Jefferis was dismissed and Strachan reinstated the following year. While under the cloud he spent his leisure instructing the Carmelite missionaries.

In 1622 Strachan was transferred to Gombroon, that is the modern Bandar Abbas, and was employed in getting ready a house, establishing a factory, and waiting to take charge of the silk convoy which was about to arrive. Except for the statement that in November of that year he suffered from a severe attack of fever and returned to Ispahan, and that he was then superseded by a regular medical officer of the Company, history is silent about the rest of his life. Possibly he returned to Europe. Certainly he intended to do so, for he commissioned Fr. Vincent, a Carmelite Father, to take to Rome sixty-one of his books written in Arabic, Persian, and Turkish, and he promised to pay the cost of their transport as soon as he himself reached Rome.[4] In the archives of the Order is Strachan's Will in which he bequeathed these books to the Carmelite Convent in Rome. In the Library at Naples to-day there are several manuscripts with their titles inscribed in his handwriting.[5] In the British Museum,[6] too, are to be found translations into Latin in the small and neat handwriting of Strachan himself of two Persian philosophical works. On the first page of one of these is written "Universum seu ut Persae vocant Poculum Mundi: Opera Georgii Strachani Mernensis Scoti in Latinum idioma traducta 1634". This book was discovered not in Europe but in Baghdad, so that the question of Strachan's own return to Europe remains doubtful.

His religion, his irregular qualifications and the complaints which were lodged against him, made it undesirable to retain him on the nominal roll of the Company. The

[3] India Records O.C. 939. [4] Chron. Carm. Per., i, 235. [5] Asiatic Quart. Rev., 5, 312, 1888. [6] Brit. Mus. No. Ms. Add. 7720, ff. 63 *et seqq.*

Minutes of a meeting[7] in Surat held in March 1621 record that Thomas Quince, who had been sent out for service at Surat, "though there bee already a suffitient surgeon", was therefore despatched in the following year to Persia "for excuseinge the chardge and supplyinge the place of an unnecessaire phisition ther entertayned".[8]

It is clear that from this time on there was a regular English physician attached to the factory at Gombroon, though I think he was the only English doctor in Persia. The Company's agents inland were not supplied with medical advisers. Neither was one included in the suite of Sir Dodmore Cotton, the first British ambassador to the Persian Court, who arrived as the representative of Charles I in 1626. For Herbert,[9] an attaché, has left an account of the ambassador's death at Qazvin and makes no mention of any British physician being in attendance. Later,[10] when he himself fell ill, he "wanted not the advice and help of the archiater, the King's doctor; who albeit he was doubtless a very skilled physician, yet did me little good, so malignant was my distemper; albeit I took what he prescribed (part of which I well remember were pomegranite pills, barberries, sloes in broth, rice and sundry other things) and returned what he expected: so that it was hard to judge whether my spirits or gold decayed faster". He was ultimately cured by a Tartar woman servant who for her fee robbed him while asleep of his clothes and money.

In 1633 Quince was succeeded at Gombroon by Constantine Young who was hurried out to Persia on account of the excess of sickness in the Factory. A few years later the Factor at Ispahan, mindful perhaps of the recent death of the British ambassador, appealed for the appointment of a surgeon there too. But the President and Council refused the request, remarking that a surgeon was unnecessary as "fevers and fluxes, both in India and Persia, are most familiarly cured by natives of each or either, to whome nor meanes nor skill is wanting".[11]

In the autumn of 1660 Young was replaced at Gombroon by Richard Brough, who did not stay very long, for the Diary records that Stephen Flower, the Agent in Persia, was accompanied by one Thomas Boyce, as Surgeon, when he travelled up from Gombroon to Ispahan in 1668.[12] In this same year the Minutes of the Court of Directors in London record that a Mr. Samuel Carlton was entertained as Surgeon for Persia at a salary of 45/- a month. He was also granted by the same Court the sum of £5 to spend upon fresh provisions, presumably for the crew of the ship which was to carry him out. Next year his salary was raised to 50/- a month. But he received no benefit from the rise, for his mother complained to the Directors at home that it was not paid to him.[13]

Although it was the determined policy of the East India Company to station its medical officers only in the Persian Gulf, still Western Medicine was not unrepresented in the big inland towns. Very soon after their arrival the Carmelite Fathers realized that a great deal of evangelical influence, not to say political prestige, could be gained by treating the bodies of the Persian nobility. In consequence the majority of the missionaries whom Rome sent out, received first a course of elementary medicine.

The first who could be dignified by the name of scientist was Fr. Matthew of S. Joseph. While he was at Shiraz he practised among the Persians and the Dutch traders.[14, 15] Later in India he gained a reputation as a botanist. At his feet sat the greatest of all the Carmelite physicians, who is especially deserving of note because he is probably the first European student of Oriental Medicine. This was Fr. Angelus of S. Joseph whose name in the world was Joseph Labrosse.

Joseph Labrosse was born at Toulouse in 1636, entered the Order of the Discalced Carmelites and took the name in religion of Angelus of S. Joseph.[16] In 1662 he went to Rome, where he studied Arabic. In the winter of 1664 he reached Ispahan and began to study Persian under a Carmelite Father of that city. Spurred on by the success of Fr. Matthew of Shiraz, who used Medicine as a means of propagating Christianity, Fr. Angelus determined to add a knowledge of Medicine to the detailed knowledge that he had now acquired of Arabic and Persian.

He returned to Paris and in 1680 he published his *Pharmacopœa Persica*. "Opus

[7] Factory Records, Surat, i, 25. [8] Sainsbury. English Factories in India, p. 237. [9] Herbert. Travels (Broadway Series), p. 208. [10] *Ibid.*, p. 221. [11] Sainsbury. English Factories in India, p. 351. [12] *Ibid.*, p. 41. [13] *Ibid.*, 41 and 43. [14] Chron. Carm. Per., i, 362. [15] *Ibid.*, i, 334. [16] Raphael du Mans. Estat de la Perse en 1660, p. ciii *et seqq.*

missionariis, mercatoribus, ceterisque regionum orientalium lustratoribus necessarium, nec non Europæis nationibus perutile" as he says on the first page.

Appointed Visitor to the Carmelite Convent in Amsterdam in 1681,[17] he succeeded in buying the oriental type which belonged to the heirs of the Elzevirs. He was thus able to publish his *Gazophylacium linguæ Persarum*, a dictionary of Persian words translated into Italian, Latin, and French. It appeared in Amsterdam in 1684. Chardin, who at this time was the Agent in Holland for the English East India Company, read through some of the proofs before the work appeared and very highly commended it. Hyde, of Queen's College, Oxford, the greatest English orientalist of the seventeenth century, on the contrary formed quite a different opinion.[18]

Although the *Gazophylacium* is not exclusively scientific, far more attention is paid to medical words than to others. It is moreover enriched with interesting little notes about any word which would be useful or unknown to ordinary students. Of Atishak, that is Syphilis, for instance, he writes that Persian authors call it the French Disease. "Nay, rather, it should be called the Persian or Turkish Disease, for there is scarcely one person in a thousand who is unaffected by it."

About this time the condition of the East India Company was now flourishing. A happy combination of circumstances had enabled them to oust their greatest rival, the Portuguese, from the shores of the Persian Gulf. The foundations of Portuguese prosperity had been laid when Albuquerque captured the island of Hormuz in 1514 and reduced its ruler to the rank of a vassal. Not unnaturally the Persian shahs considered the island to be a part of their empire although in fact their rule had always been disputed. When therefore Shah 'Abbas decided that the time had come to reassert his claim, the Company by no means unwillingly lent him their armed forces. Such a move brought advantages to both Persians and English.

The fort was taken by the combined Persian and English forces in 1622. Surgeon T. Wilson, who was on board one of the British ships, wrote[19]: "The city of Ormuz was of great bignesse, the Houses all built of stone, and seemed a most famous thing to look upon from the ships, with steeples and towres. They had fair and large churches in it, strong and stately buildings; the castle of Ormuz was the fairest, largest, and strongest that ever I saw."

In 1676 one of the really great physicians, whom the Company were fortunate to employ, was sent out to India. This was John Fryer. He was born about 1650, educated at Trinity College, Cambridge, and qualified in 1672. He offered himself to the East India Company and was accepted. "We have entertained Mr. John Fryer as Chirurgeon for Bombay," wrote the Directors in London, "at 50/- per month to commence at his arrivall, and have furnished the Chirurgery Chest now sent according to the directions of Mr. Ward."

When Fryer arrived he found that he was supernumerary and was not really required. He was thus easily persuaded by the Company's Agent [of Persia "representing how highly conducive to the Company's interest one of my Profession would be there"][20] to put in the first few months of his service in the Factories of Persia instead of in India.

He accordingly sailed on February 18, 1677, in a vessel called the *Scipio African* in the company of a young Franciscan friar who had been almost bled to death by the physicians of Goa in their efforts to save his life. On March 22 the party landed without any misadventures at Gombroon. Fryer and the agent set out for Ispahan on June 28, which they reached on August 7,[21] "having accomplished a tedious Journey in the hottest Season of the Year over desolate parching Sands and naked Rocks . . . seven hundred miles, which we performed in thirty two Days, abating the Time for Refreshment, and One Day for our Excursion to Persepolis."

Fryer at once set out to explore the city. He was first attracted by the Druggists, who lived round the Gate which led to the Armenian Bazaar. These he found to be [22] "all Jews, who are very numerous, and live apart, though their Shops are in common with the Natives in the Buzaars, mixed among a Crowd of other tradesmen; who sell by Retail and pass without any Brand, having their Synagogues open every Sabbath Day". Other writers have remarked upon the great number of pharmacies which abounded in Ispahan in those days. Herbert,[23] who had visited the city a few years before Fryer,

[17] Chron. Carm. Per., ii, 797. [18] Raphael. Estat de Perse, p. civ. [19] Curzon. Persia, ii, 417. [20] Fryer. Voyages, ii, 149. [21] *Ibid.*, ii, 177, 209 and 244. [22] *Ibid.*, ii, 247. [23] Herbert. A Relation of some Yeares Travaile 1638. (Broadway Traveller series), pp. 129 and 245.

wrote that there was no lack of "the knowledge of herbs, drugs, and gums, the Mydan in Spahawn abounding in Singular variety, and than which, no place in the world can more aptly be termed a Panacaea, a Catholicon of Herbs, of drugs: a Magazein 'gainst all diseases".

Of colleges, mosques, and Christian churches Fryer has a lot to say, but of hospitals nothing. Father Raphael du Mans, who was in Ispahan at the time of Fryer's visit, says that every large town had one or two hospitals. He even makes special mention of the hospital of Ispahan, saying that it was a large, square building with a cloister into which all the wards, large and windowless rooms, opened. It was not very much used, for when he visited it he found there only one moribund Indian lying on the floor and in another room a solitary madman chained to the wall. It was so unpopular among the townsmen that it was referred to in conversation as the Dár-ul-Marg or Death House.[24]

Of the hospitals of Shiraz, too, Fryer makes no mention. But he does remark that at a little village twenty miles north of Gombroon, where there were some natural hot-water springs, there were two "handsome hospitals . . . neat and durable works".[25] These were not Persian foundations, but were built one by the Dutch and the other by an Indian banker in the service of the English Company. The springs were still being used for therapeutic purposes a hundred years later, for Dr. John Parker, a Surgeon of the Company at Gombroon, was sufficiently interested to use them and to take some of the water back to England. On analysis it was found that sulphur was the active principle.[26]

Fryer[27] and the sub-agent left Ispahan in January 1678. With them was a French surgeon bound for Bundar-i-Rig. Though I have nowhere found his name mentioned, on chronological grounds I am inclined to identify this Frenchman with the surgeon whom Shah Sulayman dismissed from his Court for refusing to turn Mussulman. The Shah wanted two singing boys castrated for his use within the harim. He called the French surgeon in and offered him a large fee. The Frenchman accepted the offer and quite successfully operated on both. When he asked for his fee, he was bidden first turn Mussulman. On his refusal the Minister of Court "bid him begone like a Rascal, telling him withall that he did not think the Religion of the Christians had permitted such acts of Villany".[28]

At Shiraz the party was further enlarged by a Georgian soldier and a French Carmelite friar who travelled with them the rest of the way to Gombroon. Possibly this friar was the Fr. Angelus already mentioned, for it was in this year that he returned to France.

From January to April Fryer remained in Gombroon. After the arrival of the new Agent, John Petit, they set out for the interior. They reached Lar on May 8, and there most of the company fell sick. The Europeans were too prostrate to sit their horses and were carried on in litters or kajavehs. This latter is a large panier, slung in pairs on either side of a horse or camel.

The party remained in Shiraz until the end of May. The Agent then decided to push on to Ispahan, but at the earnest request of a Spanish Carmelite, resident at Shiraz,[29] who had "been long grieved with a continued Fever and finding no relief from the Country physicians", the Agent left Fryer behind to attend to him and to the English residents in the city. Scarcely was the Spaniard recovered when Fryer himself fell sick. While he was still convalescent he was summoned to treat the Governor of Shiraz. To please the Carmelite and the Armenian Christians whose welfare depended so much upon the favour of the Governor, Fryer consented to be carried out to his palace. "Whereupon my Attendance is engaged, and a Million of Promises, could I restore him to his Health, laid down from his Wives, Children, and Relations, who all (with the Citizens, as I could hear going along, pray to God that the Hackin Fringi, the Frank Doctor, might kill him) play'd the Hypocrites, wishing his Death; the first to compleat the Expectation of what he might leave them, the other for his being a Plague to them; as it proved after his recovery, for they performed as much as he, dismissing me with a Compliment, and no other Reward."

On July 6, Fryer was sufficiently recovered to continue his journey, and he set out for Ispahan. Again he did not stay long. The port of Gombroon required the presence

[24] Raphael. Estat de Perse, p. 219. [25] Fryer. Voyages, ii, 329. [26] Ives. Voyage, p. 199. [27] Fryer. Voyages, ii, 315. [28] Tavernier. Travels in Persia, v. 8, 219. [29] Fryer. Voyages, ii, 344.

of another Englishman during the "time of shipping" and the Agent being obliged to remain in Ispahan as he had failed as yet to secure an interview with the Shah, Fryer returned alone to the coast. The news of his arrival when he reached Shiraz, was at once conveyed to the Governor, who expressed a desire to have some more of the medicine which had effected his cure in the spring. But Fryer having received no fee for his former services would not attend him again.

Fryer proceeded to Gombroon where he fell ill again, and on the last day of November he returned to India,[30] "being forced by sickness to leave Persia and thereby becoming destitute of employment". For a short time he remained in Surat and then came back to England. Here he became an M.D. of his university and in 1697 was elected a Fellow of the Royal Society. What is of greater interest is that he published his observations upon the internal state of Persia. He discusses the climate, the Court, the people, and their customs. He also devotes a few pages to the state of Medicine as he found it.

With the departure of Fryer for India there is a gap in the medical records of the Factory. The Diary contains frequent entries of illnesses, deaths, petitions for sick leave and so forth, but no doctor is mentioned by name. From other authorities it is known that a doctor named Engelbert Kaempfer was in practice for a short time at Gombroon. This man, born in 1651 at Lemgo in the County of Lippe, had reached Persia in 1684 in the capacity of secretary and physician to the Swedish ambassador to the Court of Shah Sulayman. On the return of the ambassador to Europe Kaempfer went south and became physician to the Dutch Fleet in the Persian Gulf. He made Gombroon his headquarters and here he stayed until driven out by fever. On his return to Europe he published his impressions of Persia.[31] An interesting side-light is thrown upon the origin of this work by a manuscript now in the British Museum.[32] It is entitled "Descriptio Persiae communicata Dno. Engelberto Kaempfero, Ispanae, 1684, cum grammatica linguae turcicae". A dedication at the beginning of the manuscript states that it was written by Raphael du Mans, who was the Superior of the Capuchin Mission in Ispahan in those days.

The next mention of any Englishman practising in Persia that I have been able to discover occurs in the Gombroon Diary for 1727. A certain Dr. Anthony Forbes was now in charge of the health of the Factory. By this time a small hospital had been built upon which there was a monthly expenditure of 160 shahis. As the expenses of the House amounted to 5,487 shahis a month, the treatment provided for the sick can hardly have been lavish.

Economy was the watchword of the Company. The medical service felt the screw first. The drugs supplied were of a poor quality and insufficient. Dr. Forbes was compelled to report that he had "examined ye chests of Physic that came by ye Fort St. George Galley and was much surprised to find most of it useless all ye Elect. Pills, Vol. Sp. & Salts being quite dry'd up and perfectly mouldy". And a few years later he wrote:

> "Wee have not had any good or proper medicines in the Factory for the whole Season particularly Bark and every man in the Factory sick of Feavers but have been obliged to purchase them from Dutch & Eur. ships at Extravagant rates not withstanding wch. these Articles have not exceeded above per mensem 100."

In the year 1738 occurs a very interesting entry in the Diary, for it may be the earliest reference to the crippling effect of Plague in the Gulf which was henceforth to play such an important part in the political relations of Persia with India and Europe.

> "February 1738. Monsieur Vigoreux Commander of this ship gives a miserable account of Bussorah, half of the inhabitants being carried off by the late sickness and no manner of trade stirring."

Dr. Oliphant was now Factory Surgeon. He did not stay very long for after only five years of service he applied for a discharge on the grounds of ill-health and was succeeded by a Mr. John Rose. He, poor man, stayed an even shorter time, for on the morning of October 28, 1740, he died of a "Putrid Continual Fever".

In the following year Robert Herriott was appointed to Gombroon and again a severe epidemic, certainly either plague or cholera, broke out.

[30] Factory Records Surat, iv, 2, 6. [31] See Raphael. Estat de Perse, p. xc.
[32] Brit. Mus. Sloane Collection, No. 2908.

> "June 7th. 1741. News is come from Cong of a pestilential sickness having raged there to such a degree that there were hardly found people in Health to bury those that died, amounting as some say to forty & fifty a day."

The Diary relates that so fever-stricken was Gombroon in the year 1743 that after the death of the Factor from "a bilious Fever after an illness of five days" there was no European left alive in the cantonments except the Agent and the doctor.

I do not know what was the end of Dr. Herriott, whether he died at his post or whether he got back to Europe before it was too late. These next few years were terribly severe upon the health of all the Europeans of the Company. The doctors stayed only a few months before they died or resigned. Even the ships' crews did not escape.

> "October 28th. 1751. The detachment of soldiers on board the Mamoody daily falling down with fevers, which the Officers represent is owing to their Way of living being only allowed Rice, Doll, and Ghee which is very improper food for this Season of the Year, ordered them a small quantity of Pepper, and other spices to mix with their Food."

Dr. Parker, who was now the Factory doctor, made some attempt to investigate the cause of the high death rate and sickness incidence at Gombroon among the European staff. Dr. Boerhaave of the Dutch East India Company held that it was due to the intense heat of the sun being reflected by the salt encrusted in the soil. Local opinion attributed it to the stink of decaying blubber fish which were cast up on the shore in great quantities in the hot weather. Ives, a Surgeon in the Royal Navy, who visited the Persian Gulf about this time, claimed that it was malaria. I think he was right.

In 1773 Ives published the diary of his travels in these parts under the title of *A Voyage from England to India*.[33] The third appendix of this book is an account of the diseases incident to Gombroon "contained in a letter from an ingenious physician who resided several years in that settlement". This letter, although as printed is without a signature, is, I am sure, from the hand of Dr. Parker. For in it the writer states that he was "a living witness of an Autumnal Fever which began and continued almost perfectly regular for thirteen months in my own person". This agrees with another letter dated May 19, 1758, written and signed by Dr. Parker at Gombroon and now preserved in the India Office Library. In it he applies for leave on the grounds that he has been "attacked about 10 months ago with a violent Bilious Inflammatory Fever which continued for fifteen days & then terminated into a Quotidian Ague, which remained with me several months . . . and scarce had I recovered from that but was seized with a slow Continent Fever which now hangs on me".[34]

It is quite clear that Ives drew his views about malaria from Parker, for the latter writes that he was compelled to use large quantities of "the Bark", which he speaks of as "this noble medicine". This produced a shortage of drugs in the Factory Dispensary and almost in the words of his predecessors Parker wrote and complained to the Directors of the parsimony which was starving his hospital. The better health of the Dutch Factory he ascribed to other reasons, chiefly to the better conditions of living afforded by the Dutch Company.

On his departure in May 1758 Parker was presented with Rs.200 as a present for his attendance upon the Persian nobility of the town of Gombroon. He was succeeded by a ship's surgeon named Mr. Richard Mainwarring, whose duties he undertook on the return journey to Bombay.

Mainwarring was the last Surgeon at Gombroon. The place was unhealthy, and its capture and sack by the French troops in 1759 forced the Agent to recommend its abandonment. The excessive demands of a Governor of Lar two years later made the Court of Directors come to an immediate decision to close the Factory and in 1763 it was moved to Bushire.

[33] Ives's Voyage, p. 498. [34] Factory Papers. Persia, 19, 5, 1758.

The Case of Augustus d'Este (1794-1848): the First Account of Disseminated Sclerosis

By Douglas Firth, M.D.

Introduction

The manuscript from which this account was extracted was found amongst some papers in one of the London Sector Hospitals, and was written by Sir Augustus Frederick d'Este, a grandson of George III. He gives a vivid account of his own complaint, disseminated sclerosis, the clinical picture including transitory blindness and diplopia, absolute loss of power of locomotion followed by almost complete recovery, so that "the Chamois hunting" could be followed later, the gradual onset of paraplegia, tremors, sphincter troubles and sensory symptoms. The recital is the more remarkable, as the period covered, 1822 to 1846, is at least twenty years before any description comparable to this appeared in the medical Press. The names of many well-known doctors of the period are to be found in the account, as well as interesting details of various forms of treatment.

The manuscript book will be deposited in the library of the Royal College of Physicians, together with a few explanatory notes.

"In the month of December 1822 I travelled from Ramsgate to the Highlands of Scotland for the purpose of passing some days with a Relation for whom I had the affection of a Son. On my arrival I found him dead.—I attended his funeral:—there being many persons present I struggled *violently not to weep*, I was however unable to prevent myself from so doing:—Shortly after the funeral I was obliged to have my letters read to me, and their answers written for me, as my eyes were so attacked that when fixed upon minute objects indistinctness of vision was the consequence:—Until I attempted to read, or to cut my pen, I was not aware of my eyes being in the least attacked. Soon after I went to Ireland, and without any thing having been done to my eyes, they completely recovered their strength and distinctness of vision.—

In 1825 I sometimes saw imagined spots floating before my eyes. I consulted Mr. Alexander who was of opinion that I might occasionally be so troubled, but that my sight was in no danger.—In the month of January 1826 the most painful Chapter up to that period of my life occurred. I was beset by afflictions on all sides. My eyes were again attacked in the same manner as they had been in Scotland. Dr. Spangenberg sent me to Driburg, a Watering place where I drank Steel-water, bathed in it, and douched my eyes with it:—my eyes again recovered.

In June 1827 I found my Mother in bad health at Lausanne; the heat of the country I found intolerable.—My Mother and I travelled to Venice. To my surprise I there one day found a torpor or indistinctness of feeling about the Temple of my left eye. At Florence I began to suffer from a confusion of sight:—about the 6th of November the malady increased to the extent of my seeing all objects double. Each eye had its separate vision.—Dr. Kissock supposed Bile to be the cause: I was twice blooded from the temples by leeches:—purges were administered: One Vomit, and twice I lost blood from the arm: one of the times it was with difficulty that blood was obtained.—The Malady of my eyes abated, I again saw all objects naturally in their single state. I was able to go out and walk.—Now a new disease began to shew itself: every day I found *gradually* (by slow degrees) my strength leaving me: I could clearly perceive each succeeding day that I went up and down the staircase with greater difficulty. When I slapped myself sharply on the loins for the time it increased my strength.—A torpor or numbness and want of sensation became apparent about the end of the Backbone and the Perineum. At length about the 4th of December my strength of legs had quite left me, and twice in one day I fell down upon the floor in attempting to go to the closed stool without assistance; I was obliged to remain on the floor until my Servant came in and picked me up. I remained in this extreme state of weakness for about 21 days, during which period I fell down about 5 times (*never fainting*) from my legs not being strong enough to carry my body. I never once fainted or had any sort of fit:—*Debility, extreme* debility was the only cause of my falling.

I now changed my Medical Advisor, putting myself under the care of a Dr. Kent, he instantly commenced a system the very opposite to the one hitherto resorted to:—Dr. Kent made me eat beef-steaks twice a day, drink London Porter and Sherry and Madeira

wines. My legs were twice a day rubbed with brushes and the torpid part of my back was rubbed twice a day (an hour each time) with a Liniment.—This new system succeeded completely. Every day I found my strength returning:—December the 14th, 15th, and 16th 1827 I was at my greatest degree of weakness; on the 25th I was able to take a short walk, and on the 21st of January (1828) I was strong enough to begin a journey from Florence (where I was during my Illness) to Rome.—On the journey I was able to walk up some steep Hills.—At Rome I continued the system recommended by Dr. Kent namely, the rubbing with flesh brushes, and the strengthening regimen. I discontinued the rubbing my back with the Liniment but my Servant used to slap me with his open hand towards the oss-sacrum.—I rode out on horseback most days, and my strength gradually returned. I never was able to run so fast as formerly, nor could I venture to dance.—

At Splugen, a small village amongst the Alps, and in its neighbourhood I remain for Six Weeks. The bracing Mountain Air of the Alps restores me so much to strength that by degrees I am enabled to take very long walks upon the mountains and to follow to a certain degree the Chamois hunting.—I could never run with my former agility and in rocky ground and in very steep places I used to complain of the feebleness of my knees. Before I left Splugen, once or twice the coming on of the torpor and want of feeling of the old place made itself slightly perceptible.—On the 3rd of September I quit Splugen: every day of my Journey I find the torpor about the Perineum and at the end of the back bone more and more perceptible: at last I get very alarmed about it—I know not what to do, whether to stop, or at Baden-Baden to try the effects of the natural Hot Baths—I resolve to go on, and reach Hannover on the —— of September. I attend the Manœuvres of a Corps of Ten Thousand men for about a fortnight. During these Manœuvres I am able to sit upon my horse for 5 and 6 hours a day but am much fatigued by it.—After the first few days I observe that my making water is attended with difficulty, particularly early in the morning, before I have had a stool, in the course of the day time the difficulty is diminished.

Immediately on my return to Hannover I consult the Surgeon Spangenberg. On the 19th of October he attempts to pass a Bougie, he finds an impediment, he withdraws the Bougie and inserts a silver Catheter with which he ruptures what he calls a slight membranous stricture.—The operation occasions me smart pain, a cold sweat breaks out on my forehead and I feel somewhat sick: some blood is the consequence but in no great quantity.—On the following day I have a Consultation between Dr. Sleiglitz and Spangenberg. They order me to take 3 times a day a decoction of herbs and flowers, and to use every day the Shower Bath.—

I remain at Hannover from the 1st of December until the 17th always bathing every morning in the Shower Bath and drinking the tea or decoction of Flowers. During these 17 days I have observed no change in my complaint. I am able to ride for three hours at a time with pleasure, or to walk for two hours without being overfatigued: but I cannot run, or dance, and even going down stairs was unpleasant to me.

On the 17th of December I commence my journey to London:—I find that sitting for even 3 or 4 hours in a carriage increases very materially the numbness of the Perineum and extremity of my back bone, and causes a *disagreeable* sleepy effect all along the back part of the legs to the feet. I find that were I to attempt to travel far of a day I should be rendered incapable of proceeding.—

1829. In the beginning of August I go down to Ramsgate, and commence bathing in the Sea. I continued bathing in the Sea until the 15th of December:—during this time I take about 52 baths.—

1830. Whilst at Ramsgate I formed a liaison with a young woman—I find in my acts of connection a deficiency of a wholesome vigor. Thinking that possibly some return of Stricture (if ever there had been one) might be the cause I applied to Dr. Courtenay. He passed his largest Bougie at his first trial. There was no Stricture—he gave me some Medicine and Pills and certainly some increase of vigor was brought about.—I continued to consult him until the end of February, he orders me to be electrified by Partington, I undergo a course of Electricity.—

(*Details over a period of years omitted. They deal mainly with treatment*)

June 19th, 1843. What I complain of now is 1st.—that sitting produces a numbness all down the back part of my Thighs and Legs, and gives me a curious numb sensation in the lower region of the Belly.—2nd.—When standing or walking I cannot keep my balance without a Stick.

My digestion I believe to be good. I sleep well when I am not annoyed with little nervous Twitchings in my Legs or Feet, which sometimes, but seldom, is the case.—

I am naked every morning for about 30 minutes during which time I sponge myself with Cold water upon the Bidet, take Gymnastic Exercise, and sip slowly about one Pint of fresh water. My feet are rubbed and shampooed night and morning.—

I use generally the Hair-gloves. By kicking out with Strength I can exercise my legs well when steadied right and left by resting on a Chair and upon a Chest of Drawers.

I can walk accordingly as I am amused and interested by conversation:—when I am alone sometimes I walk for an hour without resting:—My walks in general are for three quarters of an hour.

December 1843.—About the 27th I saw Mr. John Scott and put it to him whether, if I were his own brother, he would not wish to talk over my Case with some one of his Medical Friends in whom he had implicit reliance. He acknowledged that such would be the case. I told him that the selection of the individual was completely with himself, in consequence of which on December the 29th he sent Dr. Farre, of No. 4 Charter House Square to visit me.—Dr. Farre read over this very book, interrogated me, and afterwards met in consultation Mr. John Scott.

January 1844.—On the 2nd of January, 1844 Dr. Farre called upon me, for the second time, and brought me the following Paper with its Prescription as the result of their Deliberation.—

London, January 1st, 1844.

'Dr. Farre met Mr. Scott in consultation on the case of Sir Augustus d'Este, and they are agreed as to its Nature, its Seat; and its Treatment, with some modifications, which Dr. Farre has suggested to make that Treatment more effectual.

'The disease is called Paraplegia and is either Active or Passive, Functional or Organic.—The transition from Functional to Organic disease is often very imperceptible; but in the Passive form of it, which is the form of the Case of Sir Augustus d'Este the duration of the functional form of the disease is often very considerable;—and Dr. Farre is of opinion, derived from the history of the Case, that this transition is not yet Conformed.'

January 1846.—Since my return to London on the 17th of December 1845 I have regained some of my Strength which was lost at St. Leonards; but then I suffer very much *indeed* from sharp Spasmodic pains in my Feet and Legs:—*Spasms which distress the whole* System—particularly of a Morning when I get off my Bed, and at times when dressing I am obliged to stand up—supporting myself—my Sensations seem to be awful indicators that some very sad Change has taken place, or is taking place in my System. I cannot now sit for any length of time *without the pressure of the hinder parts of my Thighs against the Chair occasioning Spasms.*—In Bed for the last 15 months I have not enjoyed the Comfort of the recumbent Position with which almost all are blessed.—I am obliged often to change my side from a feeling of Discomfort—not amounting to Pain—but *very distressing.* The feeling of my Limbs in Bed are very curious; and so contrary to the Nature of Health, that I know not how to give an Idea of it.—When I stand up now for a few minutes *my whole Column is affected* but in a *very slight degree* indeed.—My sensation around my Middle is as if my Legs, having been out of joint in the Thigh sockets, had been restored to their proper place; but still were under the Influence of the Injury which they had sustained.

I must also call the attention to the fact that for the last 12 months (since about January 1845) my Hands have become slightly sufferers from my Disease; the attention being directed to them—they feel dry, and, as I should think, the Hands of a healthy person would do, after having been for some considerable time in hot water and then dried.

January 22nd, 1846.—I place myself under the Treatment of Dr. Seymour M.D. of No. 13 Charles St., Berkeley Square. He visits me—he reads this book—He expresses it as his opinion that no organic Evil exists, and that there is no reason that he can see why I should not be made well—further he says that he has known *worse Cases than mine* that have been materially amended.

During this month (November 1846) I suffered from attacks of Bile so far serious that they occasioned to me Sensations that led me to fear that I should fall off my Chair in some sort of Fit or Faint. With regard to my Bowels—I should say that for the last *ten* Weeks, they have been in a *most unsatisfactory state*:—during that time I have scarcely ever had Evacuations unaided by slight Aperients.

On the favourable side I have to remark that the Sensitiveness of the Skin around my Hips and down my Legs is decidedly finer; for I cannot bear the friction of the Horsehair Gloves as I used to do. The substance of the foregoing Statement I sent to Dr. Seymour by Letter on or about the 20th (of November) and on the 25 I received the Answer.—In Dr. Seymour's Letter there is as follows:—'On the whole I think you had better leave off the Cantharides until We meet; but you will then have to resume it—as I feel very confident by Perseverance of an ultimate Recovery.'

(The last entry 1846.)

Monday December 17th. Having received a Present of Indian Moccassins I put them on:—and I walk in them without my Left Foot, which, some time ago always turned over outwards at the Ankle joint unless supported by a Steel Up right, showing any disposition so to do. Surely this is a decided Improvement. Thanks to The Almighty!"

Sir Augustus d'Este died early in 1848, in his 54th year. The cause of his death is unknown, but it is clear from his last diaries that his spasticity became so marked that he was unable to walk up any stairs and spent most of his time in his "chair on wheels." His spasms frequently caused broken nights, but they were not the only reason of his insomnia, for one entry reads: "During the past Night, I suffer from Bugs and Spasms. *I get up sadly late*".

Section of Urology

President—T. E. HAMMOND, F.R.C.S.

[*February* 27, 1941]

Case of Contracted Bladder (shown for Discussion on Treatment).—TERENCE MILLIN, F.R.C.S.

This man, aged 51, has undergone several operations during the past seven years.

Résumé of past urological history.—1934: Investigation in Brazil *re* urinary frequency and dysuria; said to show stone in prostate. Came to England for operation.

1935 (January-July): No stone found; internal urethrotomy and urethral dilatations for stricture.

1936 (January): Stone, size of pigeon's egg, removed suprapubically from bladder in Brazil; neck of bladder resected with endothermy needle; wound broke down and secondary suturing employed; lengthy convalescence.

1936 and 1937: Dysuria and frequency continue despite urethral dilatations, vesical lavage, &c.

1937 (October): Endoscopic resection of bladder neck plus bilateral vasostomy and vesicular lavage.

1937 (December): Recurrent attacks of right-sided pyelitis.

1938 (June): 30 small stones passed *per urethram* despite negative cystoscopy previous week (? prostatic in origin).

1938 (August-September): Returned to England still complaining of intense frequency and strangury. Seen by me and treated with sulphanilamides, mandelates, several dilatations of the bladder under anæsthesia (maximum capacity under general anæsthesia 3½ oz.). Transplantation of ureters into pelvic colon advised but rejected by patient.

1938 (November): Operation in Birmingham, where remnants of prostate were removed by open endothermy. Incontinence followed, which slowly improved with 85 daily irrigations of bladder through catheter.

May 1939-February 1941: Symptoms persisting. Patient seen by different urologists, including myself, who advised operative measures.

Present condition.—Has to wear a portable urinal owing to extreme frequency and urgency (amounting often to incontinence). On many days has strangury necessitating analgesic drugs. Urine swarming with staphylococci and colon bacilli. Cystoscopic examination shows a residuum of ½ oz., a maximum capacity of 2½ oz., no diverticulum, distorted bladder without much trabeculation. Intravenous urograms show relatively normal renal pelves and calices; left ureter normal; right ureter dilated in lower third (this dilatation has not increased in past four years). Blood urea is 38 mgm.% and general health good.

My own advice is now, as it was two and a half years ago, that transplantation of the ureters is indicated if the patient finds his present condition intolerable.

Discussion.—Mr. CLIFFORD MORSON, supported transplantation of the ureters if the patient's condition was intolerable.

Messrs. KENNETH WALKER and LOUGHNANE advocated a suprapubic cystostomy.

The PRESIDENT strongly deprecated cystostomy in such a case, such contracted inflamed bladders being intolerant to catheters. He was in favour of transplantation of the ureters.

Messrs. E. W. RICHES, NELIGAN and MCOUSTRA spoke in favour of transplantation.

Mr. ALEX. ROCHE said he felt the advisability of advocating transplantation depended on the surgeon's mortality for the operation.

Mr. MILLIN replied that he, like the President, felt that a suprapubic tube would make the patient's plight worse. He was glad that the consensus of opinion was in favour of transplantation of the ureters.

Collection of Stones from Bladder.—O. E. J. McOustra, F.R.C.S.Ed.

A collection of twenty-two stones, the largest of which was 1¼ × 1 × ½ in., was shown for two reasons: (1) Because it was the largest collection of stones that the exhibitor had ever seen formed in the comparatively short time of eleven weeks; and (2) to illustrate the importance of keeping the urine highly acid for a long period after prostatectomy.

History.—Rev. M., aged 55. Two-stage prostatectomy.

Second-stage, 16.3.40. Pathologist's report: Simple adenoma.

Convalescence uneventful. Wound healed in twenty-four days; patient passing urine five to six times a day and two to three times at night, with no difficulty. Was on a hexamine and acid mixture all the time, and told to continue this when he got home.

Progress satisfactory for about eight weeks. Then patient began to complain of marked frequency and pain. He is a highly neurotic man, and had refused to take his medicine as it gave him indigestion.

30.8.40: Cystoscopy under general anæsthesia. Bladder normal except for mild general cystitis. Given copious fluids and hexamine mixture, and left the home in a few days, passing urine four to five times a day and once at night.

No further trouble for about seven to eight weeks, and then began to complain of frequency again. Frequency rapidly increased, and by the end of eleven weeks from the cystoscopy he was passing urine with great pain every ten to fifteen minutes. He still persistently refused to take his medicine, and the doctor reported that his urine was alkaline.

Cystoscopy again 14.11.40, exactly eleven weeks from the previous examination, when the collection of stones was seen, and they were removed suprapubically.

During the last two to three weeks the patient has complained of further pain and marked frequency, and was cystoscoped on February 26, when another collection of about eight stones was seen. This occurred in spite of the urine having been kept acid during the last fifteen weeks.

Subcapsular Fibroma of the Kidney.—H. W. S. Wright, M.S., F.R.C.S.

This tumour was discovered accidentally in the course of a pyelolithotomy. When the kidney was exposed there was an oval, yellowish-white tumour situated on the convex border just below its mid-point. Its long axis was about 1½ cm. Its surface was slightly lobulated and it appeared to involve the renal capsule. It was thought to be an early hypernephroma, and after some hesitation the kidney was removed.

Macroscopic examination: Cut surface was slightly lobulated, rather soft, and showed some small hæmorrhages. It was about the size of a small cherry.

Section (Dr. Cuthbert Dukes): A vascular fibroma containing some adrenal tissue.

Professor W. D. Newcomb states that small fibromata are possibly the commonest renal tumours. No exact statistics are available because many of them are situated in the cortex and routine multiple sections would be necessary for their discovery. Fibromata of this size are very rare, large fibromata are rarer still and may be among the largest non-malignant renal tumours. Gordon Taylor has reported one weighing 20 lb., in fact the largest on record.

Tuberculosis in an Enlarged Prostate.—H. W. S. Wright, M.S., F.R.C.S.

History.—P. E., aged 54, admitted to hospital on 24.6.40 with clot retention of urine. He complained of occasional attacks of urgency of micturition for ten years. Lately there was difficulty in starting and his stream was poor.

Per rectum the prostate was considerably enlarged, elastic, and not indurated. Vesicles, vas, and testicles normal.

After catheter drainage renal function returned to the lower limits of normal.

Cystoscopy: Both lateral lobes of the prostate enlarged.

Operation (3.7.40).—The prostate was enucleated very easily by the suprapubic route.

Section (Dr. Walther): The cut surface showed the ordinary appearance of an enlarged prostate. The section showed evidence of tuberculosis. It showed in part the appearance of an adenomatous prostate and between the alveoli there was considerable round-celled infiltration and some typical giant-cell formation.

Progress.—Convalescence from the prostatectomy was slow and was interrupted by a staphylococcal infection of the bladder. The wound was healed a month after opera-

tion. On the sixth day after operation the temperature rose and he complained of pain in the right wrist-joint; there was marked synovitis round the radial aspect of the joint, most of the involvement being on the dorsal aspect. X-rays showed nothing to account for this. Radiological appearances were indefinite until 8.11.40, when an irregular cavity appeared in the medial aspect of the lower end of the radius, involving the radio-ulnar joint and the radiocarpal joint. The subsequent course, both clinical and radiological, has been typical of a tuberculous wrist-joint.

Subsequent examination.—No evidence of tuberculosis of the genito-urinary tract.

FIG. 1 (*Case* I).—Pyelogram showing dilatation of the upper calyx and a pelvic filling defect.

Two Cases of Carcinoma of Renal Pelvis.—E. W. RICHES, M.C., M.S.

I.—Papillary Carcinoma.

History.—H. P., male, aged 55. For four years had attacks of pyrexia once a fortnight. Asthma and bronchitis. Five months previously painless hæmaturia, followed by recurrent attacks—sometimes preceded by pyrexia. One attack of pain in right loin.

Clinical examination.—No abnormal physical signs in abdomen.

Excretion urography: Left kidney normal. Right kidney: Dilatation of upper calyx and a filling defect in the pelvis.

Pyelography: Right kidney, 12 c.c. Filling defect suggestive of new growth of pelvis (fig. 1).

Urine: Left contains transitional cells. Right contains collections of transitional cells with areas of papillary overgrowth.

Operation (11.9.40).—Right nephrectomy.

Specimen: Right kidney; pelvis filled with exuberant papilliferous growth.

Section: The greater part of the growth is a transitional-cell papilloma, but at one part of the base there is invasion of the kidney substance by solid masses of transitional cells.

Progress.—Temperature normal from the tenth day. Five months later there had been no return of pyrexia.

II.—Spheroidal-cell Carcinoma.

History.—C. L., female, aged 63. For three months attacks of pyrexia with loss of weight. Some bronchitis. Two months ago one attack of painless hæmaturia.

Clinical examination.—A little tenderness in the left loin.

FIG. 2 (*Case* II).—Pyelogram showing poor filling of the middle calyx and a pelvic filling defect.

Excretion urography: Right kidney normal. Left kidney : Upper calyces not well outlined.

Pyelography: Left kidney, 20 c.c. Upper and lower calyces dilated; filling defect in pelvis (fig. 2).

Urine: Contains a few red cells and pus cells. Sterile on culture.

Operation (20.12.40).—Left nephrectomy.

Specimen: Left kidney. Central part adjacent to pelvis 1¾ in. diameter replaced by firm white growth.

Section: Invasion by undifferentiated spheroidal-cell carcinoma.

Progress.—Temperature subsided after operation and there have been no further attacks of pyrexia up to two months later.

These two specimens both show new growths of the renal pelvis; the patients presented themselves with attacks of pyrexia as the main clinical feature. There was no urinary infection to account for it, and although in each case there was bronchitis, the pyrexial attacks ceased after nephrectomy. Decomposition of blood-clot was a possible cause in Case I, but not in Case II.

In reply to a question Mr. Riches said he did not make a routine practice of removing the ureter in pelvic new growths ; although vesical implants did sometimes occur he did not think they were sufficiently common to justify this step, and it was not always possible to tell whether the neoplasm was pelvic until the kidney had been sectioned. He referred to a case of carcinoma of the ureter shown to the Section five years previously in which, although the whole ureter had been removed, there had been repeated implantation growths in the bladder which had been kept in check by cysto-diathermy.

Parenchymatous Carcinoma of Calculous Pyonephrosis.—ALEX. E. ROCHE, F.R.C.S.

History.—Woman aged 69, thin and pyrexial, with dryish tongue and temperature varying daily from about 98° to 100°. She had had a left-sided hemiplegia three years previously. Her symptoms, complained of for about four months, were pains in the left flank, frequency and oliguria, occasional incontinence, feverishness at nights, loss of weight, pallor, weakness, anorexia, and constipation.

On examination.—There was a movable, but not tender, swelling below the left ribs. X-ray and uroselectan films showed multiple stones in a functionless left kidney. The urine contained much pus and numerous *B. coli*, the blood urea was 35 mgm.%, and cystoscopy showed much pus and a puffy pink left ureteric orifice, the right being normal. The right ureteric urine was free of pus and organisms.

Operation.—After four weeks' medical treatment, including blood transfusion, improvement permitted exploration on 23.3.38, when a coconut-sized rounded lump was found, and the colon peeled off it. On peeling condensed perinephric fascia off the lump anteroinferiorly, points of oozing pus appeared. The kidney was freed from the normal-looking suprarenal, but posteriorly the kidney was toughly adherent. Attached to it postero-externally was a spleen-sized lump of growth apparently burrowing into the posterior abdominal wall. There was similar growth in the pedicle. Nephrectomy was performed.

Pathological report (Dr. R. G. L. Waller): "A firm yellowish tumour, approximately spherical, and $4 \times 4 \times 4$ in. in size, at the upper pole of the kidney and extending into the pelvis ; there is a backward extension into the perinephric tissues, its size being about $3 \times 2\frac{1}{2} \times 2$ in. The appearances are those of a carcinoma, the cells of which to some extent resemble those of renal parenchyma." The lower half of the kidney was a series of cavities containing watery purulent fluid and stones. The discovery of growth was a complete surprise at operation.

Subsequent history.—The patient's temperature settled within a week, and deep X-ray therapy was begun a fortnight after operation; 10 applications were given, although the prognosis seemed a race between growth and another stroke. Growth won, for, a month after operation, there was a swelling of the size of a bantam's egg in the skin at the front end of the incision. The patient, obviously sinking, wished to go home, and left hospital five weeks after operation, dying two days later.

Retroperitoneal Sarcoma Causing Varicocele.—ALEX. E. ROCHE, F.R.C.S.

History.—Man, aged 54, tall, well-nourished, was admitted complaining of six weeks' swelling of the left testicle.

On examination.—There was a marked left varicocele and a large firm dull mass, moving on respiration, filling the left loin and reaching anteriorly to the mid-line—presumably a renal neoplasm, though there was no history of hæmaturia. There had been no abdominal pain. X-ray films of the chest were negative for secondaries. The psoas shadow was obscured on the left side. Uroselectan films showed no evidence of left-sided secretion at five minutes, and only faint and enlarged shadows at fifteen and thirty minutes.

Operation.—On 20.6.40, a week after his first visit to hospital, a left paramedian transperitoneal incision was made, with T-extension into the left loin, and division of the

left rectus muscle. A large rounded mass was found, encapsuled, cystic, and very thin-walled anteriorly. This portion burst, thin bloody fluid escaping. The rest of the mass was solid and adherent posteriorly, where growth was cut through in freeing it from the posterior abdominal wall. The left kidney was also removed, of which only the upper half or so could be felt, sitting on the top of the lump, and embraced and obscured by it. The kidney and ureter were afterwards found to be slightly dilated from obstruction, but otherwise normal. But, until section after removal, the mass was still mistaken for a large growth of the lower pole of the kidney.

Pathological report (Dr. R. G. L. Waller): "The neoplasm is a sarcoma; in places the appearances are those of a fibrosarcoma, elsewhere those of a spindle-cell sarcoma or those of a mixed-cell sarcoma in which the cells are large and polygonal. Numerous areas of degeneration are present; there is no indication as to the tissue from which this tumour arises."

Subsequent history.—The patient was given two courses of deep X-ray therapy, one while in hospital. Five months after operation he looked well and fat, his varicocele had vanished, he had put on two stones in weight, and had resumed work as a head gardener. But a mass, about 2×2 inches in length and width, could be felt deeply in the left loin; a further course of X-ray treatment was instituted. Three weeks later, the patient complained for the first time of neuralgia in the left thigh; on January 9, 1941, the loin lump was larger, and, eight months after operation, he is now again in hospital. (He has since died—March 1941.)

The age of this patient seems unusual for a sarcoma. The case illustrates the importance of examining the abdomen in the event of the sudden development of a varicocele, especially at, or after, middle age. Further, in this and also in the previous case there was definite typical movement of the lump on respiration; although the lumps were fixed posteriorly, their respiratory rocking on their site of attachment was indistinguishable from normal movement on respiration. Therefore, while a fixed lump is almost certainly irremovable, mobility on respiration, while strongly in favour of removability, by no means proves it.

Lymphadenoma of the Bladder.—KENNETH WALKER, F.R.C.S.

Male, aged 19, admitted to St. Bartholomew's Hospital with lymphadenoma of the cervical glands.

History.—He complained of great frequency of micturition, dysuria and, on one or two occasions, hæmaturia. There was a urethral discharge in which no organisms could be found. The main feature was intense pain, the patient being aroused twenty or thirty times a night to pass urine. The symptoms were entirely out of proportion to anything that could be found wrong with the genital tract.

Cystoscopy: He was cystoscoped under an anæsthetic and nodules the size of a grape-seed, greyish-yellow in colour, were found scattered over the bladder mucosa. A course of deep X-ray therapy brought complete relief, and later cystoscopy revealed a normal bladder.

Comment.—Mr. Walker said that lymphadenomatous deposits had been found in the bladder, post mortem, before, but that so far as he was aware this was the first time that it had been diagnosed and treated during life.

The following were also shown:

By T. E. HAMMOND, F.R.C.S.

Renal Calculi (Radiographs); Psoas Abscess (Radiographs); Staphylococcal Disease of Testis. *(Specimen).*

By CLIFFORD MORSON, O.B.E., F.R.C.S.

A New Bladder Irrigator.

By A. WILFRID ADAMS, M.S.

Radio-transparent Calculous Anuria (Stone and Radiographs)

By CECIL A. JOLL, M.S.

Adrenal Neoplasm. *(Specimen).*

Section of Comparative Medicine

President—C. H. ANDREWES, M.D., F.R.S.

[*February* 18, 1941]

DISCUSSION ON FLUOROSIS IN MAN AND ANIMALS

Professor T. J. Bosworth: Whereas acute poisoning of animals by fluorine compounds occurs but rarely and is usually accidental, the chronic form has been shown to cause extensive losses among live stock living under natural conditions in certain parts of the world. In addition, isolated outbreaks have, from time to time, been reported from industrial areas. There are records which show that the symptoms have been observed for centuries but the part played by fluorine in their production has been clearly established only within the last thirty years.

Occurrence

(*a*) *Volcanic areas.*—The disease has been observed in Iceland from early times following the periodic volcanic eruptions experienced in that country. Animals grazing on herbage contaminated by the fallen ash became affected in varying degrees depending on the extent of the contamination to which they were exposed, and many fatalities resulted.

In a collection of bones and teeth from sheep which died following an eruption which occurred in 1845 Roholm (1937) recognized gross changes which were typical of fluorine intoxication and found that the bones had a very high fluorine content. He also pointed out that fluorine may be emitted by volcanoes in other parts of the world, though there appears to be no record of intoxication of animals resulting from their activity.

(*b*) *Areas rich in phosphate deposits.*—El Darmous is a term which was originally applied to a condition affecting the permanent teeth of horses, cattle, sheep, as well as human beings in certain parts of Algeria, Morocco, and Tunis, where there are rich deposits of mineral phosphate. The drinking water which has passed through these beds is charged with fluorine, which is also found in considerable amounts in the soil in these regions, the dust from which contaminates the herbage. Intoxication from these sources leads to changes not only in the teeth but throughout the skeletal tissues, where they may become so advanced that instances of the occurrence of spontaneous fractures in horses and mules have been reported.

Extensive phosphate deposits are also found in many other parts of the world, notably North and South America (Florida, Tennessee, South Carolina, California, and the Argentine), West Indies and several South Sea Islands. Here again mottled enamel of the teeth of both human and animal populations is commonly observed owing to the high fluorine content of the water. In the isolated areas in this country in which similar dental changes have been observed among children, no cases in cattle have yet been recorded.

(*c*) *Industrial contamination.*—The discharge of fluorine by factories which utilize raw materials containing this element has been the source of a number of outbreaks among stock grazing in the neighbourhood. Among the industries which distribute fluorine in their effluents, presumably in the form of hydrogen or silicon fluoride, are those producing superphosphate, hydrofluoric acid, aluminium, copper, and other metals, glass, enamel, and bricks. Evidence suggestive of fluorine intoxication among animals grazing in the neighbourhood of superphosphate works has been observed in Italy, France, and Germany, near aluminium works in Switzerland, Norway, and Italy, and in the vicinity of other industrial plants in Germany. Recently an outbreak of a similar kind arising from the manufacture of bricks has occurred in this country.

In all of these cases which were fully investigated fluorine was shown to be the responsible agent. Excessive amounts of it were found in the herbage and in the bones of affected animals and, moreover, an identical train of symptoms was produced experimentally by feeding either fluorine compounds or hay from the pastures concerned.

(*d*) *Other possible sources of intoxication.*—(*i*) The use of mineral phosphate as a cheap substitute for bone meal in animal feeding has been tried. Samples from some districts contain too much fluorine and have been proved to be really harmful; in others the percentage is much less and does not appear to have caused any ill-effects when fed for long periods. Care in the selection of samples is therefore necessary. (*ii*) Reports from the Continent indicate that the lees from distilleries which use hydrofluoric acid or alkaline fluorides to limit fermentation by extraneous bacteria may be harmful when fed to stock.

Occurrence of the condition in this country.—An outbreak of fluorine poisoning on farms in the neighbourhood of brickworks has recently been investigated by Mr. Blakemore, Dr. Green and myself. The badly affected farms were so situated, having regard to the prevailing winds, as to be exposed to the greatest amount of smoke from the brickyards whereas pastures on the opposite side of, but equally close to, the yards were being grazed by stock with no obvious ill-effects. The inference that fluorine was being distributed with smoke from the chimneys was borne out by analysis of samples of herbage collected at various points around the works and was fully confirmed by other methods.

Symptoms in cattle.—Within a few weeks of being turned out to graze on badly affected farms, the animals showed signs of unthriftiness and some looseness of the bowels and soon developed a stunted appearance. Signs of lameness appeared within three or four months and gradually became more marked. When the cattle were housed and fed partly on concentrated food they showed some improvement, but soon became worse on returning to pasture and many of them were eventually disposed of on account of severe lameness and emaciation. The development of symptoms was especially rapid in the case of cows in milk owing presumably to their heightened calcium metabolism. In the later stages of intoxication the main symptoms were emaciation, lameness, and obvious enlargement of the bones, especially the jaws, metacarpals, and digits. Palpation revealed exostoses of the ribs and in one case there was gross deformity of the chest due to the spontaneous fracture of several of the bones. The animals tended to remain recumbent and were evidently in pain when forced to move. Difficulty in locomotion was increased by overgrowth of the hooves which was quite common. A high proportion of the animals bred on the affected farms, irrespective of the presence of other signs of intoxication, showed teeth changes identical with those referred to as El Darmous. The enamel was studded with small, irregular, whitish areas; the surface was roughened and pitted and showed patches of brownish or blackish discoloration. Owing to abnormal wear the free borders of the permanent incisors were rounded instead of having sharp edges as they normally have in the ox, and the size of the teeth was reduced, so much so in one case that on first inspection they looked like a set of milk teeth. The wear in the molars was more irregular than in the incisors, but the resulting deformity had not reached an extreme stage in any of the cases examined.

Lesions.—Apart from general signs of cachexia no changes were observed post mortem which could be attributed definitely to fluorine intoxication other than those present in the bones and teeth. Some workers have described changes in the parenchymatous organs which were regarded as more or less specific effects of the action of fluorine; in several severely affected animals which we examined nothing definite was observed in the liver, spleen, kidney, or intestine, and microscopic preparations revealed no changes beyond what might be found in a state of inanition arising from any cause.

In advanced cases all the bones of the skeleton were visibly affected but particularly the ribs, sternum, vertebræ, lower jaw, and digits. They were thicker than normal, some of them appearing quite massive, and their specific gravity was reduced. The marrow was reddish in colour and gelatinous and the marrow cavity enlarged. The epiphysial lines appeared to be normal. The ribs could be broken in the hands without the aid of a fulcrum. In one case they were so fragile that several of them broke under the slight manipulation involved in dissecting them from the vertebræ.

When the bones were macerated and dried they were seen to have lost their normal smooth glistening appearance and showed irregular, chalky-white porous deposits on the surface, pieces of which could be rubbed off with the finger.

Apart from the formation of considerable amounts of poorly calcified new bone from the periosteum, the main histological features were extensive atrophy of the bony tissue and the presence of excessive amounts of osteoid. This is in conformity with the findings of other workers who have pointed out that chronic fluorine poisoning in animals leads to changes similar in type to those of osteomalacia.

Other species of animals.—Definite signs of illness resulting from fluorine intoxication were observed by us only among cattle and we could obtain no evidence to suggest that other species of animals were clinically affected. It would appear, therefore, that cattle are more susceptible than other farm stock to the effects of fluorine. In one flock of breeding ewes many animals showed typical dental changes of fluorosis but otherwise appeared to be in quite good health, although they had been kept for a long time on pastures which were sufficiently contaminated to have caused obvious bone lesions in cattle. Cases showing affected teeth were also found among horses but no other symptoms of the condition were observed.

REFERENCE

ROHOLM, K. (1937), " Fluorine Intoxication ". London.

Dr. H. H. Green: The outbreak of industrial fluorosis in animals discussed by Professor Bosworth was investigated from the chemical point of view on material sent from the Institute of Animal Pathology at Cambridge to the Veterinary Laboratory of the Ministry of Agriculture at Weybridge, or collected on visits to the area concerned. Examination of bones showed the usual high fluorine content (up to 1,500 parts per million on the ash) characteristic of advanced fluorosis, while the determination of the fluorine content of samples of urine during life (up to 41 p.p.m. on urine as passed) enabled Mr. Blakemore to follow the occurrence of fluorosis on different farms and in animals not yet showing clinical symptoms. It was possible thus to trace out the affected area. Blood samples were of little diagnostic value because of the small margin between affected and normal animals, and the very low fluorine values of the latter (below 0·5 p.p.m.). Fluorine excretion in milk was very low and merely served to indicate the absence of danger from milk of fluorosed cows.

Drinking water was eliminated as a possible source of the disorder in affected cows while pasture grass and hay were definitely incriminated, the fluorine values varying from the normal few parts per million on the dry matter up to 82 p.p.m. (even up to 180 p.p.m. in plot experiments). By a series of controlled experiments it was shown that the high values for vegetation arose by surface contamination and not by absorption through the roots from local soil naturally high in fluorine. Atmospheric contamination on an affected farm was demonstrated by analysis of air drawn through absorption tubes and this in turn traced to the flue gases from chimneys of adjacent brick factories. The origin of the fluorine was traced to the local clay used for brick making, which parted with about one-third of its fluorine content (550 p.p.m.) at the higher temperatures of the kilns. Part of this was present in an oily mist visible at the chimney tops and derived by the condensation of products driven off at lower temperatures. This drifted down on to the pastures in the direction of prevailing winds and a complete cycle of events was thus established.

There are other points of interest concerning the sub-clinical fluorosis of sheep, poultry, and wild rabbits, the transfer of fluorine from maternal ewe to fœtal lamb, and the rate of the disappearance of fluorine from the bones of an affected cow after its transfer to normal rations.

Dr. M. M. Murray: In fluorine intoxication the effective poisons are the gaseous fluorine compounds or the fluorine ion.

Local effects are met with in manufacturing processes which involve the use of fluorine-containing compounds, especially hydrofluoric acid. Irritation and ulceration of the skin and mucous membranes, especially the conjunctiva, are met with. The generalized effects may be acute or chronic. In a record of 112 cases of acute poisoning in man over a period of fifty years, 60 proved fatal and 52 survived (Roholm, 1937). These cases were the result of intentional or accidental use of fluorine-containing substances like insecticides or rat poisons. Several research chemists have died from poisoning with hydrofluoric acid via the respiratory tract. The smallest fatal dose recorded is 4 g. (McNally, 1923), but a dose of 0·2 g. has produced severe effects. The recorded symptoms are vomiting and stomach pain, a feeling of intense cold, thirst, cyanosis, and collapse with respiratory failure.

The post-mortem records from human beings are scanty. In rats we found the most noticeable feature after acute poisoning to be the hæmorrhagic and necrotic state of the whole of the alimentary canal.

The mysterious fog disaster which occurred in the Meuse Valley near Liège in December, 1930 (Roholm, 1937) was probably due to acute fluorine poisoning. Certain gaseous compounds, HF and SiF_4, were liberated by factories in the area and there was at this time an unusually heavy fog. Several thousand persons suffered acute pulmonary attacks and sixty deaths were reported.

Chronic poisoning in man occurs in two ways, as an occupational disease and as chronic endemic fluorosis. The occupational fluorosis occurs where workers inhale or ingest dusts from fluorine-containing minerals, or fumes of fluorine or its compounds. Till recently this has been thought of slight importance in this country. Roholm (1937) has published an extensive review on the poisoning of factory workers in Copenhagen where cryolite Na_3AlF_6 shipped from Greenland is broken and powdered ready for the production of aluminium. The outstanding feature of his cases was osteosclerosis; all the bony system was affected eventually, but the vertebral column and pelvis were affected first and the most severely. The frequency of the symptoms is given in Table I. In addition there was drooping of the head and a lack of mobility of the vertebral column.

TABLE I.—FREQUENCY OF SYMPTOMS IN FLUOROSIS (ROHOLM, 1937).

	No. men	No. women	Total	Per cent. of 68 workers examined
Gastric symptoms, mainly acute (lack of appetite, cardialgia, nausea, vomiting)	42	13	55	80·9
Intestinal symptoms, mainly chronic (disposition to diarrhœa, constipation)	15	8	23	33·8
Symptoms from circulation or respiration (shortness of breath, palpitation, cough, expectoration) ..	23	12	35	51·5
Symptoms from bones, joints, and muscles (feeling of stiffness, indefinite or localized rheumatic pains)	18	6	24	35·3
Symptoms of nervous character (tiredness, sleepiness, indisposition, headache, giddiness)	12	3	15	22·1
Skin symptoms (rash)	8	0	8	11·8

The X-ray examination of the skeleton revealed osteosclerosis in degrees which varied with the time of exposure of the worker. Three phases were recognized, and these are given in Table II.

TABLE II.

Length of time employed	Condition of the osseous system as judged by the X-ray examination
2½ years	1*st phase* of osteosclerosis seen in the pelvis and vertebral column. Coarse and blurred trabeculæ, diffuse increased density of bone.
4½ years	2*nd phase*. Increased density and blurring of contours in pelvis and vertebral column, extended to ribs and extremities.
11 years	3*rd phase*. Greatly increased density of bone. Irregular and blurred contours. All bones affected, particularly the cancellous bones. Extremities thickened. Considerable calcification of ligaments of neck and vertebral column. Diffuse pulmonary fibrosis.

The teeth showed a high incidence of caries and neglect; in one young worker only was mottling of the enamel seen. Since it is obvious that fluorine has a special effect on calcified tissues it is interesting to note the fluorine content of these tissues in normal persons and in cases of fluorine intoxication. Table III shows that there is an increased concentration in bones and in teeth in fluorosis, although the increase is not great if compared with the effects which are seen.

TABLE III.—FLUORINE CONTENT OF TEETH AND BONES.

	Enamel percentage	Dentine percentage
Normal non-mottled teeth (London)	0·025 F	0·025 F
Mottled teeth (Maldon) ..	0·032 F	0·073 F
Cryolite workers' teeth (Copenhagen) ..	0·20 F	0·83 F
Normal bones, age 1 year (London)	0·03 F	
Normal bones, age 40 years (London)	0·20 F	
Cryolite workers: bones average	1·00 F	

Chronic endemic fluorosis is acquired mainly from the water supply, and the most commonly observed symptom is "mottled enamel" of the teeth of the second dentition. This condition was first studied as a water-borne disease by Black and McKay (1916) in the U.S.A. There are degrees of mottling and: "The defect exists in various stages of severity and consists sometimes of minute white flecks or yellow or brown spots or areas scattered irregularly or in streaks over the surface of the tooth. The condition may involve the whole tooth, when it presents a dead opaque, paper-white appearance. The surface is often pitted. In about 40% of cases a staining of the enamel also occurs, but whereas the mottling and pitting are present when the teeth erupt the stain is not. The stain is a chocolate brown colour and penetrates into the enamel, it can be present only or to a much greater extent on the labial aspects of the front teeth" (Black). It is a form of hypoplasia of a characteristic type and the teeth are very brittle. Williams (1923) found that this hypoplasia was a failure in the development of cementing interprismatic substance; the enamel prisms are also incompletely calcified and have the appearance of enamel from unerupted teeth. Ainsworth (1933) showed that the dentine was poorly calcified and there were many interglobular spaces. Mottled enamel is very permeable, due probably to the fault in interprismatic substance. There is a consensus of opinion that it is not more susceptible to caries, but when caries does occur the enamel destruction is more rapid and extensive and repair more difficult because of its frailty. It was many years after the original observations on mottling had been reported that the cause was proved to be the fluorine in the water supply (Churchill, 1931, 1932). The only significant study in England was made by Ainsworth (1933), who examined the teeth of children in Maldon and the surrounding districts in Essex. Mottling occurs when the water contains more than 1 part of fluorine per million (Smith, 1935) and the well water at Maldon, at the time of Ainsworth's investigation, was 5 parts per million. Casual inquiries show that the inhabitants of the Maldon district believe rheumatism and arthritis to be prevalent and it has been reported to me that school children sustain bone fractures more frequently there than elsewhere. Lantz, Smith and Leverton (1935) could establish no difference in the calcium and phosphorus balances between children with mottling and without. Marshall Day (1940) examined children with severe mottling and could find no general disturbance of any kind, though in the older members of the same population there was a high incidence of "stiff back and other skeletal changes". Shortt *et al.* (1937) reported from India the calcification of ligaments, tendons and fascia and the impairment of kidney function, but these changes only set in after thirty or forty years.

Some experiments have been designed to show the effects of small amounts of fluorine on early bone development (Glock, 1940). Chemical and histological examinations showed that there was delay and some disorganization of calcification of the bones of suckling rats, whose mothers received 0·05% fluorine in the diet. The general effects of giving Maldon water concentrated ten times to older animals are given in Table IV.

TABLE IV.—EFFECTS ON YOUNG RATS OF THE ADDITION OF MALDON WATER (CONCENTRATED 10 TIMES) TO A COMPLETE DIET.

(1) Retardation of growth.
(2) Characteristic changes in the teeth, loss of normal pigment. Teeth opaque and brittle. Increased curvature of incisors.
(3) Bones brittle, easily fractured.
(4) Degenerative changes in the alimentary canal, some digestive disturbance.
(5) Increased water intake and diuresis. In kidney, glomeruli normal, tubules affected. Mild nephrosis.

In human beings mottling is less common in temporary teeth, and it was thought to be restricted to the second dentition. Mottling has, however, been seen in temporary teeth by Smith and Smith (1935) in Arizona and by Marshall Day (1940) in 100% of the children of the 5-7 age-group examined by him in a district in the Punjab. Mottling of temporary teeth was but rarely seen by Ainsworth at Maldon. Whether mottling occurs in temporary teeth is merely a question of the concentration of fluorine reaching the enamel-forming organ. Brinch and Roholm (1934) found mottling in the permanent teeth of two children of a female cryolite worker who had suckled the children for one and a half years when some of the permanent teeth are developing. These children must have received the fluorine in the maternal milk. Experimentally it has been shown that fluorine can be transmitted to the embryo in rats (Murray, 1936) and in dogs (Knouff *et al.*, 1936).

A final point is whether fluorine is an essential element for bone and tooth development. From experiments on animals Sharpless and McCollum (1933) deduced that it is not an essential element. The view held by some that it is essential and beneficial has given rise to its use therapeutically for various purposes; e.g. to help the healing of fractures (Michaelis, 1935) and to antagonize over-activity of the thyroid gland (Goldemberg, 1932). Recently Armstrong (1937) in Minnesota has compared the fluorine content of carious and non-carious human teeth from different mouths and the same mouth. The results obtained were as follows: Sound teeth 0·011% F., Carious teeth 0·0068% F. It was concluded that fluorine, in a certain limited concentration prevents caries, but in my opinion it is difficult on the existing data to accept this view.

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Dr. J. C. Bridge referred to the first case of fluorine osteosclerosis which occurred in this country. It was brought to the notice of the Factory Department by Dr. John Wilkie, Radiologist of the Sheffield Royal Infirmary, and led to the examination of some 30 other men. Of the first six cases examined two more were found to have osteosclerotic changes similar to the first but less marked. Dr. H. A. Krebs, Director of the Biochemical Department of the Sheffield University, with the aid of a grant from the Medical Research Council, had estimated the fluorine content of the blood and urine of these workers. This showed an increase of ten times the amount of fluorine estimated as total fluorine in the blood and urine of workers exposed to fluorides as compared with people who had not been so exposed.

Dr. John Wilkie showed radiographs of two patients which demonstrated the osteosclerotic changes due to exposure to fluorine. The first case was discovered accidentally. He was a worker in aluminium fluoride, and the radiographs showed changes in the lumbar vertebræ, pelvis and extremities. The unusual " whiteness," sclerotic changes and alterations in the trabeculæ of the vertebral bodies were demonstrated. The ossification in the muscular and membranous attachments of the long bones was not prominent in this case. The second case was that of a worker in hydrofluoric acid and the radiographs showed advanced changes in the lumbar vertebræ and pelvis. Large bossy outgrowths were present in the bones of the lower legs and in the interosseus membrane of the forearms. These changes were considered typical of an advanced case of fluorine osteosclerosis.

Neither of these cases suffered from any symptoms referable to their occupation.

The Culture of Tubercle Bacilli from Laryngeal Swabs

By E. Nassau.

(*From the Department of Pathology, Middlesex County Sanatorium, Harefield, Middlesex*)

Abstract.—In a considerable proportion of cases of pulmonary tuberculosis there is no spontaneous expectoration, especially in female patients and patients under collapse treatment. A simple and efficient method is described to obtain suitable material for bacteriological examination in these cases. A laryngeal swab, made up from a piece of wire with cotton-wool wrapped round its end, is passed down the larynx and the patient asked to cough. Two swabs are taken from each patient. The swabs are passed through sterile test tubes containing 10% sulphuric acid and 2% sodium hydroxide solutions for five minutes in each and 2 Petragnani media inoculated with each swab. The cultures are examined after five days for contamination, and after twenty-eight days for macroscopical colonies of tubercle bacilli. The results obtained in two groups of cases of 166 and 107 patients were: 37·95% and 54·20% positive cultures respectively. The highest positive figures were obtained in female patients. Thus tubercle bacilli were demonstrated in a considerable proportion of cases previously regarded as sputum-negative or having no sputum. Apart from diagnosis the method gives valuable help in judging the efficiency of treatment. The finding of bacilli in early infiltrative lesions is of considerable practical as well as theoretical importance.

Résumé.—Une assez haute proportion des tuberculeux, et surtout des femmes et des malades soumis au traitement par le collapsus, n'ont pas d'expectoration spontanée. L'auteur décrit une méthode simple et efficace pour obtenir une matière appropriée pour l'examen bactériologique dans ces cas. On introduit un tampon d'ouate enroulé autour du bout d'un fil métallique dans le larynx, et on demande au malade de tousser. Deux prélèvements sont faits sur chaque malade. Les tampons sont plongés pendant 5 minutes dans un tube à essai stérile contenant de l'acide sulphurique à 10%, puis pendant 5 minutes dans un autre contenant de l'hydrate de soude à 2%. Ensuite deux cultures de chaque tampon sont préparées sur milieu de Petragnani. Après cinq jours on examine les cultures pour voir si elles sont contaminées, et après 28 jours on recherche les colonies macroscopiques de bacilles tuberculeux. Dans deux groupes de 166 et de 107 cas, 37,95% et 54,20% de résultats positifs ont été obtenues. Les proportions les plus élevées de résultats positifs ont été obtenues chez les femmes. Donc, des bacilles ont été découverts dans une proportion assez élevée de cas considérés comme ayant des crachats négatifs ou comme n'ayant pas de crachats. En dehors du diagnostic, cette méthode est très utile dans l'évaluation de l'efficacité du traitement. La découverte de bacilles dans les lésions infiltrantes précoces a une grande valeur, aussi bien pratique que théorique.

Resumen.—En una proporción considerable de casos de tuberculosis pulmonar no hay expectoración espontánea, sobre todo con las mujeres y con los pacientes sometidos a colapsoterapia. Se describe un método simple y eficaz de obtenir en estos casos material para el examen bacteriológico. Se pasa dentro de la laringe un escobillón laríngeo construido de alambre y envuelto al cabo de algodón de rama, y se pide al paciente de toser. Se obtiene dos recogidas de cada paciente, y se hace pasar éstas por dos probetas estériles, cinco minutas en una conteniendo ácido sulfúrico de 10% y cinco minutas en otra conteniendo hidróxido de sodio de 2%. Dos medios Petragnani se inoculan de cada recogida. Las recogidas se examinan a los 5 días por contaminación y a los 28 días por colonias macroscópicas del bacilo de Koch. He aquí los resultados que se obtuvieron en dos grupos de 166 y 107 pacientes: 37,95% y 54,20% respectivamente de cultivos positivos. Las cifras positivas más altas se obtuvieron en mujeres. Así demostróse el bacilo de Koch en un gran número de casos considerados hasta entonces como negativos o careciendo de esputo. Independientemente de la diagnosis este método da una ayuda valerosa en juzgar de la eficacia del tratamiento. Tiene grande importancia práctica y teórica el hallar bacilos en precoces lesiones infiltrativas.

Resumo.—Numa proporção consideravel de casos de tuberculose pulmonar não ha expectoração espontanea, especialmente nas doentes femininas e nos doentes em tratamento de colapso. Ha um metodo simples e eficaz para obter material adequado para

o exame bacteriologico nestes casos. Um tampão laringeo, feito com um pedaço de arame com algodão envolto numa extremidade, é introduzido na laringe, mandando-se ao doente que tussa. Tiram-se dois tampões de cada doente. Os tampões são passados por uns tubos esterelisados de ensaio, contendo soluções de 10% de acido sulfurico e 2% de hydrato de sodio, durante cinco minutos, cada um, e 2 culturas Petragnani inoculadas em cada um dos tampões. Examinam-se as culturas ao fim de cinco dias para vêr se ha contaminação, e depois de 28 dias para vêr se se encontram colonias de bacilos tuberculosos. Os resultados obtidos em dois grupos de casos, de 166 e 107 doentes foram de 37,95% e 54,20% de cultures positivas respectivamente. Os numeros positivos mais elevados obtiveram-se em doentes do sexo feminino. Assim encontraram-se os bacilos de tuberculo num numero consideravel de casos, que anteriormente se consideravam como de escarro negativo, ou mesmo sem escarro. Aparte o diagnostico, o metodo é de grande auxilio em verificar a eficacia do tratamento. O encontro de bacilos em lesões infiltradas precoces é de consideravel importancia, tanto pratica como teorica.

In a certain proportion of cases of pulmonary tuberculosis it is difficult to obtain sputum suitable for bacteriological examination, there being a number of cases with no spontaneous expectoration ; this is often found in women and children. Various methods have been devised to obtain suitable material for examination from these patients. By culture and animal inoculation of the gastric contents the pediatricians have been able to demonstrate tubercle bacilli in a considerable proportion of cases. The inconvenience for the patient, the complicated technique, time and cost involved, make this method, although one of our best, unsuitable for serial examinations on a large scale. The cough-plate and laryngeal mirror methods advocated by some investigators have never been extensively used.

A method is described which has been employed for over a year at Harefield Sanatorium, the results of which seem to justify publication. The technique of securing material for bacteriological examination by laryngeal swab (LS) was originally devised by veterinary surgeons for cattle, and was used as early as 1905 by Blume in tuberculous patients with no spontaneous expectoration. By the direct examination of smears from the swab acid-fast bacilli were not infrequently demonstrated by Jessen (1927), E. Szücs (1926) in America, and Hansen (1907), Lundh (1910), Edel (1928), Huppert and Gruschka (1929), Behmann (1930) and others in Europe. In spite of its simplicity, however, this method never became extensively used. The material obtained by laryngeal swab is often extremely small, and the number of bacilli accordingly very few, thus giving little chance of success by direct films.

The use of efficient media for the culture of tubercle bacilli enabled us to grow the bacilli from the smallest amount of material. This material may be regarded as concentrated sputum undiluted by saliva and nasopharyngeal secretion and Grass (1931) has shown that by culture better results could be obtained. The technique employed by Grass was similar to that used by later investigators and by ourselves. Two later publications in which the cultural method was extensively used, are those of Schramek and Hegedüs (1935) and Böhm and Ekstein (1938). The latter employed a technique similar to ours and obtained positive cultures in 46 (20·6%) of 271 cases of clinically demonstrable pulmonary tuberculosis, which had either no sputum or had been reported as sputum negative. Similar methods, but far more complicated, have been devised by Dornick (1937) and Bezançon and collaborators (1937).

The technique employed at Harefield is simple and as follows: The swab consists of a piece of brass or chromium-nickel wire 9 inches long and $\frac{1}{16}$ of an inch in diameter, one end being flattened and spirally twisted, around which the cotton-wool is firmly wrapped. The wire is then bent to an angle as in fig. 1. A large number of swabs are sterilized in a tin container, and before use the swabs are dipped in sterile water because sputum adheres better to a damp surface and is more easily transplanted on to the media. Two swabs are taken from each patient, either by using a laryngeal mirror under direct vision, or after some practice without this guide. Each swab is passed down the larynx and the patient asked to cough, and after the swabs are taken, the two wires are stuck through a piece of paper bearing the patient's name, ward, and other relevant data. When received in the laboratory the wires are straightened with sterile forceps (sterilized by flaming after each swab) and each swab is placed for five minutes in a sterile test tube containing 10% sulphuric acid. It is then transferred to a second sterile test tube containing

2% sodium-hydroxide for a further five to eight minutes. Two tubes of media are inoculated with each swab; the surface is smeared with the swab, which is at the same time being rotated. A modification of Petragnani's medium is used and cultures are incubated at 37°C. for twenty-eight days. After four to five days the cultures are examined for saprophytes or contamination, and those which are contaminated are discarded. Cultures which show no macroscopical growth after twenty-eight days are for practical purposes regarded as negative. Colonies which are thought to be those of tubercle bacilli are filmed and their acid-fast nature verified by staining. Patients having no sputum are swabbed on two consecutive days at monthly intervals.

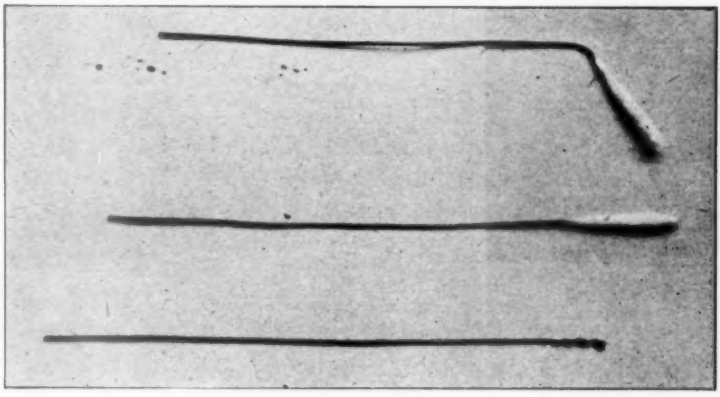

FIG. 1.

During 1940 we have examined by this method 273 patients, all of whom had no sputum at the time of examination. One group of 166 patients consists of those discharged during 1940, and a second group of 107 are still in the sanatorium. This division is helpful because it took some time to establish the method as a diagnostic routine, and in the latter group this was achieved more completely. Of the 166 discharged cases 35, i.e., 21·09%, had no sputum throughout their stay in the sanatorium, but were positive by laryngeal swab culture. Another 28 cases, i.e. 16·86%, with positive sputum on admission, becoming later sputum negative, or having no sputum, were found to be still positive by this method. Considering these two groups together a positive result has been obtained in 37·95% of cases examined (Table I). Of the 107 cases at present in the sanatorium the corresponding percentages are 35·51 and 18·69, making a total of 54·20 (Table II). In the latter group separate figures have been compiled for both sexes (Tables III and IV), and higher positive figures have been found among the female patients.

By the introduction of the laryngeal swab culture method tubercle bacilli have been demonstrated in a large number of patients who had no spontaneous expectoration, and particularly in cases under collapse therapy and in those with early infiltrative lesions. The finding of bacilli in these latter cases is to be regarded as a definite sign of activity and is bound to influence our therapeutic indications to a considerable extent thereby widening the field of collapse therapy. Spontaneous expectoration often ceases after the introduction of an artificial pneumothorax, and in these cases the efficiency of the treatment can be conveniently gauged by repeated laryngeal swab cultures, particularly when, as is frequently the case, radiological findings are indefinite. The indications for additional measures may be greatly influenced by the results of the cultures.

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TABLE I.

Cases	Number of patients	Percentage of patients
No sputum throughout sanatorium treatment. L.S. culture + ...	35	21·09
Originally sputum positive; later no sputum. L.S. culture + ...	28	16·86
Originally sputum positive; later no sputum. L.S. culture —	35	21·09
No sputum throughout sanatorium treatment. L.S. culture —	68	40·96
TOTAL	166	100·00

Cases discharged during 1940.

TABLE II.

Cases	Number of patients	Percentage of patients
No sputum throughout sanatorium treatment. L.S. culture + ...	38	35·51
Originally sputum positive; later no sputum. L.S. culture + ...	20	18·69
Originally sputum positive; later no sputum. L.S. culture —	18	16·83
No sputum throughout sanatorium treatment. L.S. culture —	31	28·97
TOTAL	107	100·00

Cases in the sanatorium.

TABLE III.

Cases	Number of patients	Percentage of patients
No sputum throughout sanatorium treatment. L.S. culture + ...	26	49·05
Originally sputum positive; Later no sputum. L.S. culture + ...	7	13·20
Originally sputum positive; later no sputum. L.S. culture —	6	11·32
No sputum throughout sanatorium treatment. L.S. culture —	14	26·43
TOTAL	53	100·00

Female patients in the sanatorium.

TABLE IV.

Cases	Number of patients	Percentage of patients
No sputum throughout sanatorium treatment. L.S. culture + ...	12	22·22
Originally sputum positive; later no sputum. L.S. culture + ...	13	24·07
Originally sputum positive; later no sputum. L.S. culture —	12	22·22
No sputum throughout sanatorium treatment. L.S. culture —	17	31·49
TOTAL	54	100·00

Male patients in the sanatorium.

Section of Epidemiology and State Medicine

President—J. ALISON GLOVER, O.B.E., M.D.

[*March* 28, 1941]

Pulmonary Tuberculosis in the Royal Navy and the Use of Mass Miniature Radiography in its Control

By Surgeon Rear-Admiral SHELDON F. DUDLEY, C.B., F.R.S.

IN early reports on the health of the Royal Navy, pulmonary tuberculosis was included under many headings, such as " phthisis ", " consumptive diseases of the lungs ", " cachexia pulmonis ", " expectoration of blood " and " hæmoptysis ". Tuberculosis of the lungs has always been an occupational disease of seamen. As long ago as 1780, Sir Gilbert Blane said that as many as 218 men suffering from " consumption " had been admitted that year to Haslar hospital alone.

According to a volume containing the statistical records of the health of the Navy from 1830 to 1836, the Mediterranean Fleet reported 285 cases of " consumptive diseases of the lungs " and 147 cases of " expectoration of blood " during these seven years. As the average strength of the fleet was about 8,000 men, these figures represent a case incidence of about 8 per thousand per annum. Of these cases 105 died during the period, representing a case fatality of about 25%. Practically all these entries must have referred to tuberculosis of the lungs. But the recorded case incidence may have exaggerated the number of men who contracted tuberculosis ; because the recorded incidence often refers to the number of entries on the sick list rather than to the number of individuals suffering from the disease mentioned. However, this fallacy is offset by the certainty that there must have been a fair number of tuberculosis cases entered under other headings, especially under the fever groups, and a group labelled " chronic inflammation of the lungs ". Even should the recorded incidence figures have exaggerated the incidence of pulmonary tuberculosis, the case fatality cannot have been less than 25% for those cases recorded as consumption and hæmoptysis, because the same patient cannot die twice.

The case fatality in itself indicates the lethal nature of tuberculosis at sea a century ago. There are many conditions which are often mistaken for tuberculosis of the lungs which, before the days of X-rays and bacteriology, must have been a cause of falsifying the statistical returns. In this connexion the Mediterranean type of undulant fever is of especial interest to the Navy. In my time, the pulmonary type of Mediterranean fever was, more often than not, at first temporarily diagnosed as pulmonary tuberculosis. And, in the days before Marston differentiated the disease as a clinical entity in 1861, many cases of undulant fever remained permanently on the records as cases of phthisis. A good example of this error is given in the Milroy lectures of 1931 (Dudley). During the year 1861, while serving on the Mediterranean station, H.M.S. *St. Jean d'Acre* recorded 219 cases out of a ship's company of 880, which were finally diagnosed as " phthisis " or " cachexia pulmonis ". Only six of these cases died, the rest recovered completely, usually after a long illness. A case fatality of 3%, at a time when the fatality from phthisis was usually over 25% elsewhere in the Navy, combined with other evidence, makes it certain that these men were in fact suffering from the pulmonary type of Mediterranean fever which was able to spread by droplet infection from man to man without the intermediary of the goat, under the conditions prevailing in ships eighty years ago. In passing, note

the analogy with the pulmonic type of plague which can spread through the human herd directly without the intervention of the rat and the flea, which are necessary for the transmission of a bubonic type of plague.

The errors of false diagnosis and multiple entries of the same case in the sick list were balanced to a greater or less extent by errors due to missed diagnosis. Probably, the real incidence of tuberculosis of the lungs was about 8 per thousand per annum in the middle of the last century—a rate fourfold that which exists to-day. Since then this rate has dropped irregularly until 1906, by which time the diagnosis of tuberculosis was fairly accurate. After this year, the statistical records of pulmonary tuberculosis were more accurately kept. The graph of the so-called case incidence of naval tuberculosis shows an irregular downward trend right up to 1913, the last complete year before the last war. During the war the statistical record was discontinued and not resumed until 1921. As was fully explained elsewhere (" Anonymous ", 1938), because all cases of tuberculosis of lungs are invalided out of the Service, the invaliding rate is an accurate record of the relative incidence of the disease during any two periods. Since the beginning of the century up to the present time the invaliding rate has fluctuated round 2 per thousand. In the fourteen years 1900-1913 this rate averaged 2·2, in the fourteen years 1921-1934 the rate averaged 2·1. Therefore in spite of all our efforts to prevent tuberculosis in the Navy, during the last thirty-five years when, as judged by mortality, the amount of tuberculosis in England and Wales must have been nearly halved, the prevalence of tuberculous disease in the Navy has remained unchanged. The real decline in naval tuberculosis rates, which took place in the latter half of the nineteenth century, was parallel to the downward trend of the incidence of the same disease in the civil population. And both falls were probably due to the same natural causes, perhaps accelerated by improvements in the environment, standard of living, and medical diagnosis. The decisive factor left untouched which determines the high incidence of tuberculosis in the Navy is density of population. The work for which a warship is designed prohibits any increase in the number of square feet of deck space per man, and the density of population must increase as more space is taken up by machinery, which requires additional men to work it:

All measures that have been introduced in the last thirty-five years, namely the drive to get earlier diagnosis by periodical medical examinations and weighings of the men, the elimination of dampness and dust between decks, the great improvement in the protective qualities of the naval rations, and increase and perfection of the air supply, have not been accompanied by any decrease in the morbidity of pulmonary tuberculosis. However, it is possible that the recruits of to-day, owing to the marked fall in the prevalence of civilian tuberculosis, are more susceptible to the disease than they were thirty-five years ago, and that therefore the incidence of tuberculosis would have gone up, had it not been for these apparently non-effective preventive measures.

This speculation is indirectly supported by the observation that the boys aged 15-16 years who enter the naval training establishments have a low herd-immunity, as judged by the unexpectedly low percentage of those among them who give a positive tuberculin reaction (Mantoux test).

All the work on droplet and air-borne infection suggests that by far the most dangerous and massive doses of infective material are those which are passed directly from man to man at short range, in the act of coughing, sneezing or even speaking. It is obvious that once the average distance between the respiratory orifices of the members of a community is reduced below a certain point, ventilation, however effective, cannot influence the spread of infection. Shaw (1926) lays great stress on periodical medical examinations and the weighing of men as a preventive measure in order to discover and eliminate early cases of pulmonary tuberculosis. But many sputum-positive advanced cases fail to give any physical signs at a meticulous clinical examination. Little can be hoped from periodical weighings, as loss of weight is a late rather than early sign of tuberculosis. In fact we know that scarcely any of the tuberculosis concealed in the Navy has been uncovered by these routine weighings and examinations.

This critical morbidity of 2 per thousand is double that prevailing in the Army and Air Force, although the Navy has a larger proportion of men in those younger and older age-groups who, in civilian life, show a lower incidence of pulmonary tuberculosis than the average. As far as can be judged, the naval rate is considerably higher than that in men of the corresponding age and social class ashore, although naval ratings form a specially selected group who have passed through the sieve of a medical examination and

who, except as regards air space, have a standard of living higher than that of the average working man.

Another observation, which indicates that it is the closeness of community life on the lower deck which is the determining cause of the excess of tuberculosis morbidity among naval ratings, is the fact that the yearly incidence among naval officers is 1·0 per thousand per annum, less than half the morbidity among the ratings. Naval officers nearly always sleep in separate cabins, and their day living accommodation is also more spacious. Officers being recruited from a more sheltered social group would be expected, other factors being equal, to show a higher tuberculosis morbidity than the ratings. Even still more suggestive of the beneficial effect of the more spacious life of officers, is the observation that, when men are promoted to officers from the lower deck, the rate for tuberculosis among those promoted drops from 2 to 1 per thousand. Among the men of the same age and seniority who remain on the lower deck the rate remains unchanged.

The halving of the incidence is obviously due to the increase of space and better sleeping accommodation which are the only significant differences between these two groups.

If we could remove all men with open tuberculosis from the Navy no fresh infections would be possible in the ships themselves, however congested the environment.

The tubercle bacillus only divides about once a day as compared to about every half-hour with most of the common pathogenic organisms, as for example *B. typhosum*. This may be one reason for the insidious onset of the disease, in that the infected host has plenty of time to adjust his reactions to the slowly multiplying parasite, and to develop considerable lesions before any definite signs of the disease are obvious. This allows tubercle bacilli to find their way into the respiratory discharges of their host for months or years before the patient, his messmates, or doctor realize what is the matter.

This insidious onset should help in the prevention of the disease, if we could segregate the infected men during the considerable period that elapses between infection and the time when the disease becomes " open " and tubercle bacilli first appear in the sputum.

In the Navy, in spite of frequent examinations, a sailor is rarely discovered to have pulmonary tuberculosis before tubercle bacilli have appeared in his sputum and before he has become a possible danger to his messmates. Of 93 consecutive cases of pulmonary tuberculosis admitted to the Royal Naval Hospital, Chatham, in 1938 and 1939, in only 9 were no tubercle bacilli found in their sputum ; and some of the latter cases were picked up in the X-ray room by chance when being examined for some other purpose.

As is well known X-rays are the only means of detecting the earliest lesions of pulmonary tuberculosis, and all men suspected of the disease are promptly examined by X-rays in the Navy. But it is the unsuspected cases of pulmonary tuberculosis which must be found if the large reservoir of concealed tuberculosis in the Navy is ever to be drained.

The difficulty of examinations by the ordinary X-ray methods were discussed in a previous paper (" Anonymous ", 1938). Any scheme, short of examining the total force at periodic intervals, is unlikely to have an appreciable effect on the total morbidity from tuberculosis of the lungs. If only recruits are X-rayed to prevent the introduction of fresh infections into the Navy, some cases will be found among the older new entries. Trial investigations, however, have shown that it was exceptional to find any tuberculosis among the boy seamen and artificer apprentices who enter the Navy at 15 to 16 years of age. Incidentally, it was observed in these training establishments that those boys who gave negative Mantoux tuberculin tests on entry, did not tend to become Mantoux positive before leaving the training establishments, as do medical students in hospital and the nurses in sanatoria, who have frequent opportunities of making contact with tubercle bacilli. This is evidence that little tuberculosis infection was, at the time of the investigation, taking place in the boys' and artificers' training establishments, and suggests, that naval tuberculosis is contracted more often in the ships themselves, than ashore after or before entering the Navy. Thus the X-ray examination of recruits only is unlikely to have an appreciable effect on naval tuberculosis morbidity. Moreover the Germans have been examining their recruits by X-rays for some years and their rate for pulmonary tuberculosis before the war was the same as ours, about 2 per thousand per annum.

Even if it were possible to discover and remove all tuberculous infection from one ship by means of X-ray examinations, the uninfected ship's company will be exposed to the same risks of infection again within two or three years, because a naval commission only lasts that time, at the end of which the ship pays off and its inhabitants are distributed to other ships all over the world. Therefore we are driven to the conclusion that the

incidence of pulmonary tuberculosis cannot be reduced by much, unless the total naval force is examined radiographically at periodic intervals.

With the introduction of the technique known as miniature-photo-radiography, mass X-ray examinations of the whole Navy became a less cumbrous and expensive proposition. The Medical Director General examined the possibilities of the new technique, and after Surgeon Commander Fitzpatrick had carried out some "trial runs" at a naval hospital, Their Lordships of the Admiralty gave permission to install the necessary apparatus and staff at the three main naval depots to which practically every naval rating returns at least once every three years. Therefore, as it is proposed that every man joining the depots shall pass through the miniature photoradiographic departments, all the chests in the Navy will be examined radiographically at least every three years, once the scheme is in full operation.

The new technique has been criticized on the grounds that the miniature photographs and their projections are not as reliable as full-sized films, and that cases will be missed and others wrongly diagnosed. In the Navy no man is labelled tubercular on the evidence of the miniature film until a full-sized film has been taken. If this shows evidence of progressive tubercular disease, he is sent to hospital where he undergoes a complete clinical and laboratory investigation. The function of the apparatus is to pick out, quickly and economically, as many as possible who have abnormal X-ray shadows of their lungs.

MASS RADIOGRAPHY IN NAVY.

Years service	Number X-rayed	Re-exam. Full size	Per cent. re-exam.	? Active Tb.	? Active Tb. per 1,000	S.E. ? Act. Tb. per 1,000
			Trained Men.			
– 5	4,518	140	3·1	11	2·4	± 0·73
5 +	2,439	129	5·3	20	8·2	± 1·81
Total trained men	6,957	269	4·0	31	4·5	± 0·81
Age – 30	5,224	152	2·9	12	2·3	± 0·64
30 +	1,733	117	6·8	19	11·0	± 2·48
			New Entries.			
Age – 20	2,065	51	2·5	5	2·5	± 1·1
– 25	6,240	184	3·0	16	2·6	± 0·65
– 30	2,240	116	5·2	10	4·5	± 1·41
30 +	1,249	52	4·2	7	5·6	± 2·10
Total new entries	11,794	403	3·4	38	3·2	± 0·52
			Total All Examined.			
Grand Total	18,751	672	3·6	69	3·7	± 0·44

NOTE.—In the last column S.E. = Standard Error of the rates per thousand in the preceding column. Examination of the S.E.s shows that, as yet, not enough data has accumulated for the observed differences in the frequency distribution of "? Act. Tb." to have much statistical significance.

The table summarizes the results of the first 18,751 naval ratings who were examined by miniature photoradiography. These men fell into two groups, new entries to the Service and those already trained or who had been under training for some time. For obvious reasons the new entries preponderate at the present time and are older, on the average, than the men joining the Navy in peace time. Also they do not include the youngest naval recruits, who are the boy seamen and artificer apprentices referred to previously. The headings at the top of the table require explanation. "Re-exam: Full Size" refers to men whose miniature pictures exhibited some abnormality and who were re-examined by use of full-sized films. The next column gives the percentage of those thus re-examined in the total group. The column labelled "? active Tb." gives the number of men who were, on re-examination, suspected to have active tuberculosis of the lungs and were sent to hospital for a full investigation. The last column gives the number per thousand of these suspects in the corresponding groups.

When the total new entries and total trained men are compared there is little difference between them in the percentage of individuals who require re-examination, and the rate per thousand of suspected active cases of tuberculosis was only a little higher in the

trained men. If, however, the trained men are subdivided, according to their length of service in the Navy, into two subgroups of those of less than, and those of over, five years' service, the senior group is found to have a rate for suspected active tuberculosis which is 3·4 times as great as the rate in the junior group. If the trained men are divided according to age into those of over and under 30 years of age, the elder group is 4·8 times as liable to suffer from suspected active disease.

The statistics of the trained men are not in a form to decide whether length of service, apart from age, is correlated with tuberculosis morbidity, especially as there were only 198 men over 30 years old with less than five years' service, and they only produced one suspect. But, if the new entries are subdivided into age-groups, as shown in the table, although there is no significant difference between the rates of the junior and the younger trained ratings and the rates of the younger new entries, yet the rate for suspected active tuberculosis of the lungs in the trained ratings of over 30 is twice as high as that of new entries over 30. These figures, taken as a whole, confirm the deduction that was made above from the official naval statistical returns of previous years that naval ratings are about twice as prone to develop tuberculosis of the lungs as men of similar type who work ashore.

As the figures in the table indicate, 69 cases of suspected pulmonary tuberculosis were sent to hospital. Of these cases 47 were found to have active lesions, in 20 the disease was considered to have been arrested, and these men were discharged to duty to be re-examined in three months' time. The remaining two men had no appreciable disease. The 47 patients with active disease represent a rate of 2·4 per thousand examined. Therefore the number of cases discovered by the new technique will not overstrain the hospital facilities, or make the temporary rise in the incidence of naval pulmonary tuberculosis and the extra loss of trained men by invaliding, which will result, appear unduly alarming to the uninitiated.

Of the 47 men who were invalided, 24 had tubercle bacilli in their sputum. Thus, in this group of cases picked out by miniature photoradiography, 50% were open cases, as compared with 90% discovered in the ordinary way when a man reports sick of his own accord with symptoms which suggest pulmonary tuberculosis to his doctor. This is disappointing as it had been hoped that the proportion of open cases would have been much smaller. However as time passes and the unsuspected open cases are weeded out, the ratio of closed to open cases should increase. Those 47 men, who were found to be suffering from unsuspected progressive tuberculosis of the lungs, were at full duty at the time of discovery. Most of them complained of nothing in particular, and were indignant at being sent to hospital.

The number of cases of active tuberculosis is as yet too small for the frequency differences in the sub-groups to have much statistical significance until one or two hundred thousand examinations have been completed. The personal equation and experience of the radiologist also is a factor of considerable weight, especially in deciding which men are to be re-X-rayed on full-sized films.

Apart from their primary function of uncovering the concealed foci of tuberculous infection in the Navy, the photoradiographic departments should offer a fertile field for research on the early evolution of tuberculosis and other diseases of the chest.

Conclusion

Many men who may have been suffering from unsuspected tuberculosis of the lungs for months or years are being detected earlier by this method. Therefore the chances of a permanent and rapid arrest of their disease is greater. About half of these unsuspected cases, instead of a tenth as heretofore, are "closed" cases of pulmonary tuberculosis who are removed from the naval community before they can become a possible danger to others. The other moiety of unsuspected cases were open cases who might have gone on distributing tubercle bacilli for a long time had they not been radiographed. It is also a fact that individuals picked up in this way are found to be suffering from tuberculosis earlier than they would have been if left to themselves. In the Navy, the removal of unsuspected cases will occupy two or three years. After which it is to be hoped that the tuberculosis morbidity will fall.

The success of the procedure in preventing or reducing the morbidity of pulmonary tuberculosis depends on the truth of the hypothesis that all or many of the cases of the disease in adults in this country are due to fresh infections with tubercle bacilli in adult life. But there are some who still believe that, in countries where tuberculosis is endemic,

most tuberculosis of the lungs is contracted in infancy or childhood. This early infection is generally arrested only to progress again if some unfavourable secondary factor in adult life lowers the individual's resistance to tubercle bacilli, which until then were lying dormant in the healed infantile lesion.

The second reason why mass radiography may fail to effect the results expected of it is more difficult to explain. The risk of infection can never be eliminated completely from the naval community. Odd cases of tuberculosis will always continue to be contracted ashore, missed at the X-ray examinations, or develop during the intervals between the examinations. We have no knowledge of the minimum number of bacilli, or what frequency of contact with them, is necessary to originate a progressive tuberculous lesion in a susceptible subject, under the special conditions of naval life. It is possible that the foci of infection on the mess decks of a warship are far more numerous than are necessary in order to ensure that the potential cases of pulmonary tuberculosis in the Navy get a minimal infective dose at some time during their naval service. In this event, the irreducible overcrowding of a ship's living quarters will remain the decisive factor in the incidence of tuberculosis of the lungs, in spite of removing many open cases of the disease.

In spite of the improvement in the standard of living and other hygienic measures, there has been no diminution in the frequency of naval pulmonary tuberculosis during the last thirty-five years. Therefore it is not wise to dogmatize on the ultimate effects of mass-radiography as a preventive measure.

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Mass Miniature Photoradiography in the Royal Navy

By Surgeon Commander W. G. C. FITZPATRICK, R.N.

ALL men joining the Royal Naval Barracks at Chatham, whether direct from civil life or from other ships or establishments, are passed through the Photo-Radiographic Department as part of the "joining routine". This routine includes an examination by a medical officer, and if a man makes any complaint regarding his health, or exhibits any gross lesion on clinical examination, he is immediately referred to the sick quarters proper (after the routine miniature radiograph has been exposed) where a complete examination is made and any necessary investigations arranged.

The examination is not used as a substitute for normal radiography, nor as a means of diagnosing pulmonary tuberculosis, but is merely a rapid and economical method of selecting—from a large number of presumably healthy men—cases for further examination clinically and radiographically, with the object of reducing the incidence of pulmonary tuberculosis in the Royal Navy.

The apparatus in use was supplied by Messrs. Stanley Cox of London, under the name of "Pulmograph".

It consists of:

A 10 kW. protected X-ray tube, blower cooled and with 4·8 mm. focus. A specially designed Leica type of camera (35 mm. film) with an f/1·9 Dallmeyer 2 in. lens. The camera is electrically operated—it has no shutter and the exposed frame is automatically moved on immediately the photograph of the serial number has been taken.

A light and ray proof tunnel connects the camera with a Levy West fluorescent screen 36 in. away. The tunnel has a light proof slit in the centre of its undersurface near the screen. A card—stamped with an identification number—is inserted into this slot, and is illuminated as soon as the fluorescence from the screen has faded. The identification number is thus recorded upon the film (in the mid-line of diaphragmatic region).

The camera, tunnel, screen and tube are mounted as one on a massive stand in such a way that they can be easily adjusted to the varying heights of the men.

The distance between camera and screen = 36 in., and that between screen and tube = 36½ in. (It was originally 40 in.)

An oil immersed single valve transformer with output of 120 mA. at 80 kVp.

Factors used are: 100 mA. at 75 kVp. The exposure is determined by weight in pounds and varies from 0·3 to 0·6 second.

Examination Routine

The men, who are already stripped to the waist after their routine medical inspection, come into the department. They pass in single file to a counter where they fill in the necessary particulars (name, rating, &c.) on a white card which has been stamped with the identification number.

The men, with cards, continue in file, and in strict numerical order to the apparatus.

The man stands on the step of the apparatus, his card is marked in pencil with the exposure time and inserted into the slot in the tunnel.

The man is then "positioned" as follows: (1) Chin in rest (notch on top of screen (mid-line)). Hands on hips, with elbows forward and shoulders down, so as to draw scapulæ forwards. Screen image photographed in full inspiration. (The position: "Hands on hips" is not illustrated.)

When the screen image has faded, the identification card is illuminated and so photographed in its turn. The number will be seen in the diaphragmatic region on the negative.

FIG. 1.—New entries lining up to be X-rayed in the "Pulmograph".

The exposed frame moves on automatically.

The man leaves the department.

When completely exposed, the film is removed from the camera and processed without delay. The film used at present is panchromatic and therefore must be wound on to the developing reel and placed in the light proof tank in absolute darkness. The remainder of the process may be finished in daylight. The film is developed for eight minutes at 65° F., then washed for one minute followed by twenty minutes in an acid-fixing solution. It is then washed for one hour in running water. At the end of this time the excess moisture is removed by means of a rubber sponge or woollen roll and the film is dried in a drying cabinet.

When dry the film can be viewed by the following methods:

(1) Naked eye.
(2) With watchmaker's lens.
(3) By means of projection on to a white screen.

Comments on above:

(1) Can usually detect gross lesions.
(2) Is very tiring if many strips have to be examined.
(3) Satisfactory. The projected image measures 10×12 in.

The projected images are usually quite good and lesions are readily detected in a large number of cases, but we have worked throughout on the basis that this method is not a

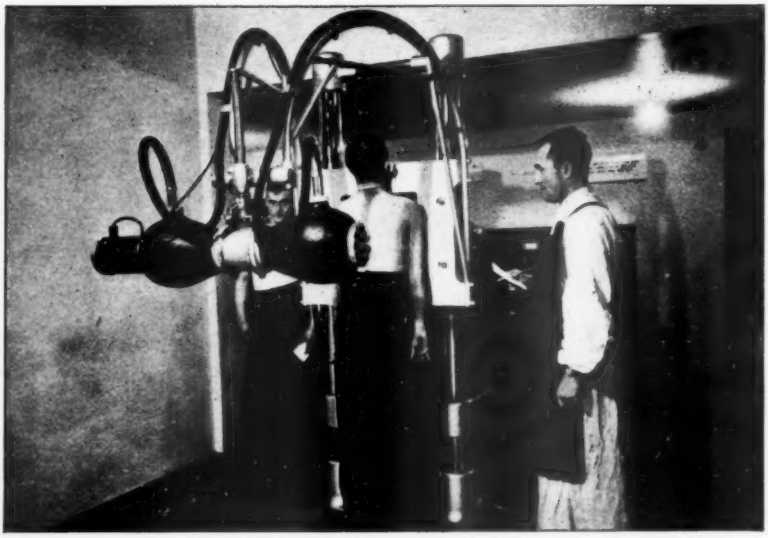

FIG. 2.—A new entry being X-rayed in the "Pulmograph", taken from the rear, showing the X-ray tube in the foreground actually in operation.

final means of diagnosing pulmonary tuberculosis. It is a rapid and economical way of picking out doubtful cases. We have exposed as many as 200 cases per hour; which is about as fast as the men can be positioned. The "frame" costs about one halfpenny.

Owing to the shortening of the distance between the patient and tube a little experience is required in order to interpret the films satisfactorily.

The distance between tube and patient being only 36 in. there is more distortion than in films taken at 72 in.

The cardiac shadow is relatively larger and not so definite in outline. An error in positioning is liable to increase this distortion.

The hilar shadows are magnified, as are the lower bronchial markings—especially on the right.

The infraclavicular striations (vascular markings) are unusually accentuated.

The apices are well defined and lesions in these, and in the clavicular zones, are well seen.

Infiltration, cavitation, calcification and pleural thickening are all well defined in satisfactory films, and can be detected by naked-eye examination.

Owing to the short focal skin distance we have found some early lesions to be better shown than in the large film.

Any case which shows abnormality in the small film at once has a large radiograph taken, and the man is examined by a medical officer. If there is any clinical or radiological evidence pointing towards a pathological condition, he is sent to hospital for full investigation.

So far we have exposed over 23,000 frames.

Large films exposed, 513. With increasing experience fewer large films were required.

FIG. 3.—Operator, wearing protective lead apron, working the control of the "Pulmograph".

All unsatisfactory films—due to faulty technique, &c.—are repeated as soon as possible. With inexperienced staff, unsatisfactory results are caused by:

Faulty positioning.
Bad loading of camera.
Processing errors.

Of 128 cases sent to hospital:

Tubercle bacilli positive = 27.
Clinical tuberculosis = 34.
Healed pulmonary tuberculosis = 6 (inactive).
Cardiac cases = 5.

Cases picked out by miniature radiography were later diagnosed as follows: Pulmonary

tuberculosis, Pneumonia, Fibrosis, Pleural effusion, Old pleurisy, Dextrocardia (3 cases), Phrenic paresis (3 cases), Hilar adenitis, Hydatid cyst, Cardiac cases, Cervical rib (3 cases), Pneumothorax, Bronchiectasis.

All cases which showed any abnormality are kept under observation and are examined after a stated interval.

FIG. 4.—The author reading a negative and reporting results.

The film is divided into strips, each containing about nine frames. These sub-strips are filed (flat) in cellophane envelopes, and are suitably indexed. Prints or enlargements can easily be made of any desired frame.

A discussion followed in which the following took part: Surgeon Commander A. R. Thomas, Dr. W. M. Crofton, Dr. Philip Ellman, Sir Wilson Jameson, Dr. D. C. Staveley, Dr. A. L. Cranch, Dr. R. Cruickshank, Dr. S. C. Shanks and Colonel W. Butler (Chairman).

[*The four figures illustrating this paper are reproduced from the "Journal of the Royal Naval Medical Service,"* **27,** 3, *by permission.*]

Section of Medicine

President—Sir Maurice Cassidy, K.C.V.O., M.D.

[*March* 25, 1941]

DISCUSSION ON DYSPEPSIA IN THE FORCES

Colonel H. Letheby Tidy: *Classification of the types of dyspepsia.*—Dyspepsia as it is met with in the Army as a whole, can be classified in three principal groups.

(1) *Peptic ulcer.*—In this group are all cases with positive radiographs. It also includes certain "negative X-ray" cases in which clinical specialists are satisfied that an ulcer has been present, as may occur with cases of gastric ulcer when the barium meal is carried out after a course of treatment.

(2) *Gastritis.*—This group is well recognized but a strict definition is difficult. The symptoms are persistent or recurrent, but radiographs are negative. The term "functional dyspepsia" would be preferable if there were agreement as to the meaning of the word "functional". If used for this group it should imply absence of demonstrable disease in the stomach and duodenum and elsewhere in the body but without other implications.

(3) *Transient dyspepsia.*—This frequently occurs among new recruits before they are acclimatized to Army routine. These men can be dealt with satisfactorily in the unit and consequently this condition should not be met with in hospital.

There is a miscellaneous group including such conditions as reflex dyspepsia due to the appendix, gall-bladder, &c., but the number of these in the Army is small.

Dyspepsia occurring as a manifestation of well-marked psychoneurosis is not included.

Malingering is rare. Exaggeration of symptoms is by no means uncommon and is not always the fault of the man. Exaggeration of symptoms tends to increase progressively with each admission to hospital, with each repetition of investigations and over-careful and conscientious inquiry into symptoms and with undue retention in hospital for treatment.

Incidence in Hospitals of Cases of Dyspepsia

In large hospitals dyspepsia will usually account for 15% to 20% of all medical cases and the proportion may be even higher, but this gives an exaggerated view of the incidence in the Army. The proportion of cases of dyspepsia to total admissions to hospital has remained fairly stationary in recent months.

What Proportion of Cases Admitted to Hospital for Dyspepsia have Proved Ulcers?

The larger hospitals get a higher proportion of the cases which medical officers in the units believe to have definite ulcers. Secondly, there is a tendency to transient dyspepsia in the recruits. This group can be properly retained in the unit, but if certain medical officers send these cases to hospital it will reduce the proportion of peptic ulcers. The figures may therefore vary considerably in different hospitals.

TABLE I.—ANALYSIS OF 2,500 ADMISSIONS TO MILITARY HOSPITALS FOR DYSPEPSIA.

	Per cent.	Per cent.
Duodenal ulcer	32·5	
Gastric ulcer	9·2	
Peptic ulcer	8·0	
Hæmatemesis and melæna	2·2	
		51·9
Gastritis (functional dyspepsia) ...		35·0
Gastro-enteritis and colitis ...		6·8
Appendicitis		2·3
Cholecystitis		0·8
Carcinoma		0·3
Miscellaneous		2·9
		100·0

Table I is compiled from 2,500 consecutive cases admitted for dyspepsia to several hospitals in different parts of the country, most of the returns covering a period of twelve months or more. The returns are not all on the same system. Certain hospitals have used such terms as "juxta-pyloric ulcers". These latter have been entered as "peptic ulcers". Duodenitis has been regarded as duodenal ulcer. Peptic ulcers constitute 51·9%. Gastritis, which accounts for 35%, will here include such cases of the group of transient dyspepsia as may reach hospital. There is a small group of miscellaneous conditions. The proportion ascribed to appendicitis and cholecystitis are in reasonable agreement with the figures given by Rivers and Pereira for the Mayo Clinic. The proportion of duodenal to gastric ulcers is about 3½:1.

Why is the Incidence of Dyspepsia in the Army so High?

There is another question which should be considered first. Is the incidence of dyspepsia higher in the Army than in civilian life? Did the dyspepsia originate in the Army or previously?

Newman and Payne in their study of cases of dyspepsia evacuated from the B.E.F. early in the War found that 92% of ulcers had originated in civilian life and only 8% subsequent to joining the Service. This result has been criticized on the grounds that the cases, though unselected in this country, had, in fact, been selected in France since only a proportion of the admissions to hospital for dyspepsia were evacuated home. Gibson Graham has taken records of cases admitted to hospital over a period of fourteen months, only a few coming from the B.E.F., and finds that 94% of ulcers originated in civilian life with a previous duration of six to seven years. Further, in the group returned as gastritis there is a history in civilian life in 79% with an average duration of seven years. Thus there is no evidence of any undue fresh development of the severer forms of dyspepsia in the Army. The low peace-time figures for admission to hospital also support this statement. These studies draw attention to the early age at which dyspepsia commences in cases which subsequently prove to have ulcers. It is often well marked in the early twenties.

What is the Incidence of the Severer Dyspepsias in Civilian Life?

There has been an enormous increase in gastro-duodenal disease in recent decades. Denys Jennings concludes that there are no statistics from which this increase can be accurately measured. Fig. 1 (*Lancet*, 1940 (i), 446, fig. 13), which is taken from his article, is constructed from the Registrar-General's Returns, and shows the annual deaths from peptic ulcer in males per million living. It will be seen that the deaths from peptic ulcer have increased severalfold since the last war. The same is also true of other countries.

With regard to the group of gastritis, there are no statistics which can give us an indication of its incidence.

The only publication as to gastric conditions among civilians during the present war of which I am aware is that of Melton in February 1940, which records that the admissions

to Lewisham Hospital, both for hæmatemesis and for perforated ulcer have doubled since the onset of war.

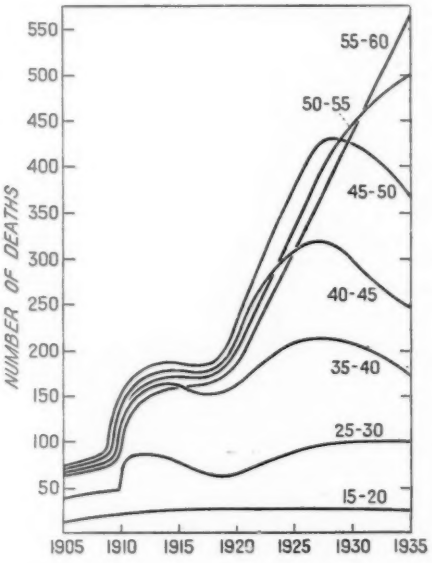

FIG. 1.—Annual deaths from peptic ulcer in males in certain selected five-year age-groups. From the statistics of the Registrar-General. The sudden rise in 1911 is due to the inclusion (for the first time) of deaths from duodenal ulcer.—(From "Perforated Peptic Ulcer" by Denys Jennings, *Lancet* 1940 (i), 446).

Do Chronic Dyspeptic Conditions Relapse more Quickly in the Army than in Civilian Life?

While it is clear that a high proportion of cases of gastritis and an even higher proportion of peptic ulcers originated before the war, the question still arises whether relapses develop more quickly in the Army than would have happened in civilian life. In the Army admissions to hospital are regarded as a relapse and all recurrences will involve such admission. In civilian life, on the other hand, men will often be treated at home for milder recurrences. Some of the men proved to have peptic ulcers after joining the Service, have had various recurrences in civilian life without entering hospital, and some have never been in a hospital, although they have been treated for dyspepsia over long periods. The frequency of recurrences in civilian life is illustrated by Bashford's study of Post Office employees. He found that 33% of cases of duodenal ulcer and 50% of cases of gastric ulcer were absent from duty for recurrences for two weeks or more every year. What passes as a slight recurrence in civilian life with a few days' rest on milk diet at home, involves admission to hospital in the Army and counts as a relapse.

Bearing in mind this difference in meaning, I think relapses have developed more quickly in the Army. There is no doubt that a high proportion of cases of peptic ulcer have been admitted to hospital within a few weeks or months of joining the Service. Newman and Payne record that men often think that the attack is the most severe which they have had.

Why do Cases of Organic Dyspepsia Relapse in the Army?

(1) *Army diet and Army cooking.*—The Army diet is more liberal, contains more meat and is heavier than the normal diet of the mass of the population. The small proportion of cases admitted to hospital for dyspepsia developing after joining the Service prove

that the diet is satisfactory for men who have not previously suffered from such condition.

Diet and cooking may be factors in the rapidity with which dyspeptics relapse in the Army, but they are not the essential cause. It is the Army routine which is incompatible with the continuous maintenance of efficient health in those who are already the subject of peptic ulcer and certain grades of gastritis.

A bus-driver, the subject of peptic ulcer, once described his routine in civilian life. His trip took eighty minutes, and between each trip he had milk or light food and frequently took Maclean's powder. His régime thus was not far different from Sippey's diet. With this routine he managed to carry on successfully with occasional sick absences for a few days or a week or so. In the Army he was admitted to hospital after a few weeks.

The unsuitability of men with peptic ulcer for the Services is no new discovery for the Army authorities. A man in peace-time may live in married quarters and take money instead of part of his ration, but it was found many years ago that if a man has a peptic ulcer he could not stand Army life and it has long been a regulation that he should be invalided out of the Service.

(2) *Influence of psychological factors.*—It may happen that in the case of a man reporting sick with complaint of dyspepsia, the medical officer, on a general survey, may decide that he is primarily a psychoneurotic and refer him to a psychiatric specialist. If he agrees the man may be discharged forthwith from the Service or sent into hospital under a specialist. I have seen a certain number of these cases thus admitted to hospitals, and, as a general physician, I would agree that they are essentially psychoneurotic and not primarily dyspeptic.

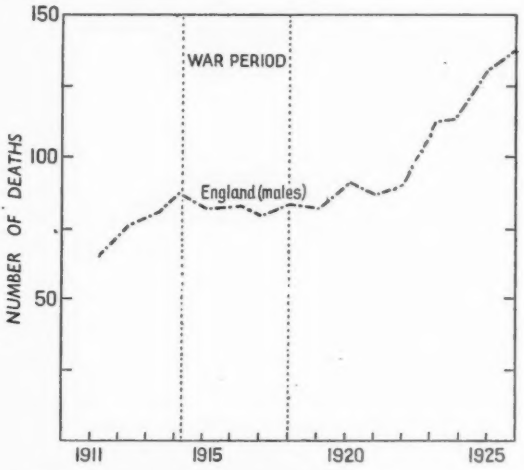

FIG. 2.—Number of male deaths in England from all peptic ulcers per million of the population (Registrar-General).—(Adapted from "Perforated Peptic Ulcer" by Denys Jennings, *Lancet*, 1940 (i), 444).

This, however, is not the whole problem. The question arises as to the frequency of psychological factors in the development or recurrence of what may be called organic dyspepsia, that is peptic ulcer and some grade of chronic gastritis.

Newman and Payne decided that there was practically no evidence of psychological factors. Certain other investigators are in agreement, but others would classify all X-ray negative cases as neurotic.

The possibility of psychological factors is obvious, including such disturbances as worry about business and separations from home and family. But one of the greatest anxieties of civilian life, insecurity of occupation, is removed, for a man cannot lose

his job, is fed and clothed and paid regularly. Attention may be directed to the acknowledged rapidity with which ulcer patients lose their symptoms under a dietary régime in hospital without any attention to psychological aspects and in contrast to the more obstinate symptoms of chronic gastritis.

The psychological disturbances present in this war existed also in the last war, with the exception of bombing which has only become important in the last few months, and hence it is not irrelevant to inquire what effect the last war had on the incidence of peptic ulcer. Fig. 2 (*Lancet*, 1940 (i), 444, fig. 6), which is also taken from Denys Jennings' article, shows the annual deaths from peptic ulcer in males per million living recorded in the Registrar-General's Returns. Fig. 1 shows that the rise had begun before 1911 and continued until 1914. Fig. 2 shows that, during the war period, the incidence was stationary or even fell slightly. After the war the rise immediately began again. Thus the rise in the annual deaths per million living was checked during the war and commenced again at its conclusion.

This is in agreement with the observations in France during the last war that peptic ulcer and all dyspeptic disturbances were noticeably rare. In the "Medical History of the War", gastric disturbances are scarcely referred to and duodenal ulcer does not appear as a separate heading in the statistics. The last war affords no evidence that the relapses in cases of peptic ulcer and chronic gastritis can be attributed to concomitant psychological disturbances. It should be realized that there is no evidence that the present war has been accompanied by any increase in the incidence of peptic ulcer or other severe gastric disturbances. What the present war has so far revealed is the unsuspected frequency of peptic ulcer and gastritis in the civilian population before the War commenced and the not surprising fact that organic dyspepsia is incompatible with Army life.

Gastritis

The group formed 35% of the 2,500 cases mentioned above, but as a representation of its frequency the figures are open to the fallacy that a smaller proportion of this group than of peptic ulcer find their way into hospital.

Graham and Kerr find that there is a history of similar symptoms previous to joining the Service in 80% of this group with an average duration of seven years. This is evidence of the prevalence in civilian life and it is possible that this condition has increased *pari passu* with peptic ulcer in recent years but, except from the limited aspect of gastroscopy, little attention has been paid to it.

The symptoms in many cases so closely resemble those of the ulcer syndrome that they may almost be described as near-ulcers. A few are undoubtedly ulcers, negative to X-rays, but this is not the full explanation. It is the common experience of civilian practice that these cases rarely develop demonstrable ulcers or the recognized complications of that condition.

Some of these cases approach the border line of definite psychoneurosis and there appears to be a greater aura of psychological factor in this group than in frank ulcers. But it is not the primary factor throughout, nor do I believe that psychiatric treatment will rid men of their symptoms. These men are not malingerers, but they rapidly become exaggerators as the result of over-investigation and treatment and the group, as a whole, requires some degree of firmness which in fact they receive in civilian life and to which they have to conform unless they are prepared to lose their occupation.

In peace-time these cases may be sent by their doctor to a hospital where they are admitted and "investigated fully". If "all investigations are negative" they are then disposed of in a third common phrase: "Sent back to his doctor." The man may continue to visit his doctor or an out-patient department, but it is important to note that in most instances he succeeds in continuing at his work.

Gastroscopy takes the investigation a step further, but at present it has provided no solution and only adds a diagnosis in a small number of cases. Gastroscopy justifies itself in many directions. Thus it can occasionally establish the presence of a carcinoma or of an ulcer not revealed by X-rays, and it can recognize that a gastric ulcer is not healed although all symptoms have passed. But when other changes in the mucous membrane are in question, gastroscopy has not yet sufficiently established the limits of normal or the interpretation of the abnormal.

In the Army a short course of treatment for men in this group is rarely successful in ridding them of their complaints, for symptoms are more obstinate and more continuous

in this group than in frank peptic ulcer. As soon as possible after the investigations are complete and after a short period of treatment, they should be sent back to their units without waiting for complete relief from dyspepsia. They may be given such advice and assistance, medical and psychological if desired, as is compatible with Army routine. It is then the function of the medical officer of the unit to keep them on duty and a number of these men do, in fact, make useful soldiers in spite of their disabilities. If the attempt to keep them on duty fails, but not until there has been a proper trial, they should be sent again to hospital and, in many cases, they should then be invalided out of the Service. Medical officers of units often fear that an ulcer has been overlooked, and some complication may occur for which they will be blamed, but in fact such catastrophes are extremely rare. A more excusable difficulty rises from the tendency to vomiting, which also occurs with peptic ulcers. A possible explanation is that the men get unusually hungry after a morning in the open air and eat too hearty a meal. In my experience, it is rare for a second investigation to be positive when the first has been negative. I would also call attention to the value of careful tests for occult blood.

Transient Dyspepsia

Judged from the figures from attendances at Medical Inspection Rooms of Training Centres, transient dyspepsia is more frequent than all the other groups together. It is not so common in hospital wards and, indeed, ought to be unknown there. We are here getting away from hospitals and looking at dyspepsia as seen in the units.

A healthy man when he joins the Army is placed in a new environment and often develops symptoms of dyspepsia about the second fortnight, for which he reports sick. A parallel is the dyspepsia which often affects healthy persons when taking a holiday in another country. An experienced medical officer recognizes the condition, reassures the man and explains it to him and gives him a bottle of medicine. This last is essential as otherwise he would be branded as a malingerer which he is not and knows that he is not. He may report sick twice in the following fortnight, once in the next and then no more is heard of him. He has become acclimatized. But a medical officer not so experienced, or lacking self-confidence, may send the man to hospital for a specialist opinion. This is the first mistake. The medical specialist should return him at once to his unit, but he may make the further mistake of admitting him to hospital for investigation, which proves to be negative. In this group, unlike chronic gastritis, the symptoms respond readily to hospital treatment and the man is sent back "cured" to the Training Centre. But although the symptoms have been removed the man has not been acclimatized and the cycle starts over again and he is then admitted to hospital a second time. It is almost true to say that a recruit who has twice been admitted to hospital within a short time for the same complaint will not subsequently get rid of the symptoms. His chance of making a useful soldier has been taken away and, further, he can claim that in the Army he developed chronic dyspepsia from which he had never suffered previously.

Table II.—Gastric Cases seen by a Medical Specialist in One Week.

(1)	Peptic ulcers	11
(2)	Admitted. Indefinite or severe cases ...	2
(3)	Returned to units: M & D	7
(4)	Recommended for discharge for conditions other than gastric	2
	Total	22

Table II is an analysis of cases of dyspepsia sent to the medical specialist of a military hospital during one week from units and records his opinion and disposal of them. Seven men were sent back to duty, most of these being transient dyspepsia which should have been kept in the unit. The return of these cases and a note from the medical specialist instructs the medical officer that he should have dealt with them himself. Two cases only were admitted. The illustration here given is a satisfactory record. If the medical work is weak the figures will be disproportionately higher in Nos. 2 and 3. When dyspepsia in the Army is discussed it is often solely on the basis of cases seen in hospital wards which only gives a partial picture. The medical officer of a training centre, especially an experienced general practitioner, sees the complete picture more correctly.

Conclusion

Men with peptic ulcer should be invalided out of the Service without delay. The diagnosis may be justifiable on clinical grounds although radiographs are normal.

Efforts should be made to keep on duty men with chronic gastritis. If admitted to hospital they should be returned to the unit after investigations are concluded without waiting for complete relief of symptoms. Many of them make useful soldiers with no greater discomfort than affects them in civilian occupations. But if the attempt fails and a man has been repeatedly admitted to hospital, he should be invalided out of the Army. Placing in a lower category is rarely effectual.

It is important that the symptoms in transient dyspepsia should not be converted into a permanent disability by injudicious handling.

A high proportion of the cases both of peptic ulcer and gastritis suffered from similar symptoms for a period of years before joining the Service and there is no evidence that the number of new cases developing in the Army is in excess of the number which would occur among an equal population in civilian life in the same time.

The incidence of peptic ulcer and gastritis in the civilian population is greater than has been realized and has increased rapidly in recent years. The establishment of a special hospital for the study of gastro-duodenal diseases is long overdue.

My thanks are due to medical specialists and others in many hospitals and especially to Lt.-Colonel Gibson Graham and Captain Kerr whose article I quoted from before publication with their permission, and to Major J. G. Scadding.

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Dr. Charles E. Newman: The investigation done by Mr. Payne and myself in the spring of 1940 showed that the bulk of the gastro-duodenal disease in the Army hospital was organic, and consisted predominantly of duodenal ulceration. The Army at that time was composed largely of Reservists, and with the change to an Army of younger conscripts the position may have altered. But it is to be expected, in view of the surprisingly early age of onset of ulceration which we found, that ulcers would still bulk largely. The figures published since then have shown a fall in the percentage of ulcers in the hospital dyspeptics from the 60% which we found to about 40%.

In doubtful cases gastroscoped by Mr. Payne, the interesting point emerged that some of those cases which we should have left in the groups of "Indefinite Dyspepsia" or "Probable Ulcer" have turned out to be either patchy gastritis, of the Alexis St. Martin type, or ulcers not visible radiographically.

I was given an opportunity to visit an Army hospital to which all the doubtful and generally unsatisfactory sick are drafted, and which might therefore be expected to show the other extreme to the organic material on which I had previously based my views. I went over twelve cases, and found that they comprised six definite duodenal ulcers, two probable duodenal ulcers, one gastric ulcer, one gastritis, and two neurotics. Although the sample is small, it suggests that there are still a large number of ulcers, but that neurotic dyspepsia has increased.

In discussing dyspepsia in the Army four main points stand out as being of practical importance:

(1) There is a tendency to overestimate the importance of radiography before a diagnosis is accepted by a Board. In our investigation, Mr. Payne and I adopted definite, but very strict criteria for the diagnosis of ulcer (we had to, because the investigation was a statistical one, and we had to separate the certain cases from those which were only presumptive). These criteria were: (*a*) a clinical syndrome of peptic ulceration; (*b*) a history of relapses and remissions; (*c*) occult blood in the stools; (*d*) a test-meal picture consistent with a diagnosis of ulcer; (*e*) a history of perforation of gross hæmorrhage, and (*f*) the radiological finding of an ulcer. The proper way to make a diagnosis is to collect and consider all the information, allowing each factor its proper weight. That is the way one works in civil practice, and it is the right way to work in military practice.

(2) The distinction between duodenal ulcer and duodenitis is a constantly recurring problem. There are local schools of thought: what one radiologist would interpret as an ulcer, is interpreted by another as duodenitis. The difficulty seems largely a matter of words: where is one to draw the line between a mucosal inflammation, a superficial loss of a few cells, a shallow ulcer, and a definite ulcer? Surely the essence of the matter is the natural history of the disease; whether it is behaving like an ulcer, or like a transient indigestion. There is no question that the crater of a duodenal ulcer may be impossible to demonstrate, at any rate without the mucosal-pattern technique, and that distortion can be caused by scarring without an active ulcer.

(3) The sharp distinction between the organic and the neurotic is often untenable. Many patients with ulcers are also neurotic, as a result of their ulcers, and it is more than likely that many ulcers are the result of psychological disturbance.

(4) There is a group of doubtful and difficult cases which can only be diagnosed by a complete investigation by every known means. The practice of discharging a man half diagnosed and half treated, so that he is constantly in and out of hospital, is a very bad one. It wastes time and money, and is demoralizing to the victim. While some doctors are interested in gastric patients, others regard them as an unsatisfactory class, with no physical signs, uncongenial personalities, long and dull treatment and a tendency to relapse. Gastric cases should be centralized and put under a medical officer interested in such work. A careful selection should be made of those which seem to warrant thorough investigation.

Major J. G. Scadding: My remarks are based upon the study of a series of cases of digestive disorder seen as out-patients at a military hospital in England during the four months September to December 1940, inclusive. Various circumstances rendered it most convenient to investigate the greater number of the patients as out-patients; relatively few were admitted to hospital. All the cases were referred for specialist's opinion by unit medical officers. The total number of cases seen thus, in the four months reviewed, with a main complaint of symptoms referable to the digestive system was 193. They may be grouped as follows:

Cases with gastro-duodenal symptoms examined by X-ray, including proved ulcers	137
Possible peptic ulcers, in which investigations were not completed for various non-medical reasons	18
Dyspepsias not considered clinically to be organic, in which no X-ray examination was performed	23
Dyspepsia after appendicectomy	6
Chronic appendicitis	2
Gastro-enteritis	2
Constipation	3
Cholecystitis	2

It is the group of 137 cases with symptoms suggesting gastro-duodenal disorder, in which either the nature or severity of the symptoms warranted barium meal examination, or the presence of a peptic ulcer had been otherwise proved that I shall discuss

The nature of the population from which the cases were drawn was quite different from that from which Newman and Payne's cases came. Owing to the large number of training units in the neighbourhood of the hospital at which I worked, there was a large preponderance of quite recent recruits in my series, and the number of regular soldiers and reservists was relatively small. Thus of the total of 137 cases to be discussed, 31 only were regular soldiers or reservists. As in Newman and Payne's series, the symptoms in the majority of cases had started in civil life. In only 25 of 137 cases had symptoms arisen for the first time during Army service; in 100 cases, the onset was in civil life before beginning service, and in 12 the patient was a reservist in whom symptoms had arisen in the interval in civil life on reserve. This preponderance of cases in which symptoms had arisen during civil life was even more definite in the case of the group of "proved ulcers" (to be defined below). Of 57 cases falling into this "proved ulcer" group, only 6 had their first symptoms during their Army service—that is, 89% of "proved ulcers" were probably present before the beginning of Army service, a figure very similar to that reported by Newman and Payne, who found that 92% of ulcers in their series had been present before the war.

ANALYSIS OF 137 CASES WITH GASTRO-DUODENAL SYMPTOMS

	Total	Proved ulcers		Stomach hypertonic		Stomach orthotonic	Stomach hypotonic	
			Previous operation	Duodenum spastic	Duodenum normal	Duodenum normal	Duodenum spastic	Duodenum normal
Number of Cases	137	41	16	24	16	5	13	22
Regular Soldiers	31	8	1	4	5	1	6	6
Officers	10	6	1	1	1	1	0	0
Average age (years)	—	31	34	$28\frac{9}{12}$	$33\frac{6}{12}$	30	33	30
Average age at onset of symptoms (years)	—	26	$25\frac{9}{12}$	23	$28\frac{3}{12}$	$27\frac{6}{12}$	$28\frac{3}{12}$	$23\frac{6}{12}$
Onset : before starting service, in civil life	100	33	15	17	8	2	7	18
reservists, onset in interval of civil life	12	3	—	2	1	1	4	1
during service	25	5	1	5	7	2	2	3
The following figures are percentages of the total number of cases in each group showing the respective features :								
Periodicity : ++	—	38	46	29	6	0	38	41
+	—	35 } 73	38 } 84	17 } 46	31 } 37	40 } 40	38 } 76	18 } 59
±	—	12	16	21	13	20	8	18
0	—	15	0	33	50	40	16	23
Pain : epigastric or hypochondric	—	88	87	71	50	100	77	64
elsewhere	—	12	13	29	31	0	23	32
nil	—	0	0	0	19	0	0	0
clear relation to meals	—	85	87	83	75	60	92	73
relieved by food	—	41	25	50	19	20	15	5
Tenderness	—	59	47	33	50	20	62	45
Vomiting : ++	—	0	0	9	25	20	38	23
+	—	29 } 29	31 } 31	18 } 27	6 } 31	0 } 20	8 } 46	23 } 46
Recommended for discharge	55 [75]	90 [37]	100 [16]	58 [14]	0	0	15 [2]	27 [6]

Since it was found that correlation of clinical history and radiological findings was often difficult, an analysis of the cases according to the radiological findings has been made. Under the heading of "proved ulcers" are included cases in which an actual ulcer crater was observed radiologically, or the presence of an ulcer had been proved at previous operation (either for the treatment of the ulcer or for perforation); I must hasten to add that for purposes of treatment and boarding, the clinical aspects of the case were also considered in arriving at a diagnosis! Using this strict criterion of the demonstration of a crater or history of operation, 57 of the 137 cases (42%) were proved to be of peptic ulcer. The remainder were classified according to the radiological findings, as follows:

Stomach hypertonic, duodenum spastic	24
Stomach hypertonic, duodenum normal	16
Stomach orthotonic, duodenum normal	5
Stomach hypotonic, duodenum spastic	13
Stomach hypotonic, duodenum normal	22

The clinical findings in these groups have been analysed in an attempt to detect some correlation with the radiological findings. First a few words about the *peptic ulcer* group. The main part of this group of 57 cases consisted of 41 cases in which no operation had been performed. In 17 of these the diagnosis of ulcer had been made previously, in civil life in 16, and earlier in Army service in the case of 1 regular soldier: in the remaining 24 the diagnosis was established for the first time at my examination. Of the 41 cases of "non-operated" ulcer, 23 were duodenal, 9 gastric, 6 pyloric; and in 3 the site was undetermined, the diagnosis in these cases being established by a report from another hospital which, while making it quite clear that an ulcer had been detected, was indefinite as to its exact site.

The remainder of the "ulcer" group consisted of 16 cases in which operations had been performed—in 12 for perforation, with or without gastro-enterostomy, and in 4 for gastro-enterostomy alone. In all but one of these "operated" cases the operation had been performed in civil life, before the beginning of Army service.

Though the figures are rather small, it may be significant that, while 57 of the whole series of 137 fell into the "proved ulcer" group, of the 10 officers included in the whole series, no fewer than 7 fell into the "proved ulcer" group.

An interesting feature, which has been noted in other series, was the early age of onset of symptoms in some of the "proved ulcers." The average age at onset of symptoms was 26 for the whole 57 cases; in 14 of them symptoms had first occurred before the age of 20. The average duration of symptoms at the time the patients were seen by me was five years in the "non-operated" group, and eight in the "operated" group. It is noteworthy, however, that similar findings with regard to the duration of symptoms, and age at their onset, were made in the cases of dyspepsia in which no ulcer was demonstrated.

Taking the "proved ulcer" group as a whole, the clinical histories obtained approximated to the classical picture of peptic ulcer. Thus well-marked periodicity of symptoms was noted in about 75% of these cases, the pain was in the upper third of the abdomen in 88%, and showed a clear relation to meals in 85%. Relief of pain by food was observed in about 35%. Vomiting was not the most prominent feature in any of them, but was a definite complaint in 30%. Abdominal tenderness was detected in 55% at the time of examination. 53 of the 57 patients were recommended for discharge from the Army, the remaining 4 being officers in favourable forms of employment.

It is an important point, however, that some of the histories obtained were far from conforming to the accepted picture of peptic ulcer. For instance, a man of 32 years, who was shown to have a duodenal ulcer, complained of five years' pain in the right hypochondrium without detectable relation to food, and with very doubtful periodicity; he vomited occasionally without relief of pain, and he was habitually constipated; there was, on examination, quite well-marked rosacea, and rather vague generalized upper abdominal tenderness. Such atypical histories were, however, the exception.

The patients with "proved peptic ulcers" presented no real problem to the Army physician: either they were in the very small minority of specially employed experienced persons who could live out and provide their own special diet, when the possibility of

retaining them in the Army could be considered, or they had to be boarded out of the Service. The real difficulty arose in those cases in which radiological evidence was not unequivocal. These will now be considered.

(1) *Stomach hypertonic, duodenum spastic.*—There were 24 cases in which the radiological appearances could be summed up in this way. Of them, 14 (58%) were thought to have a clinical history, which, combined with these suspicious appearances, justified a diagnosis of duodenal ulcer, and these were therefore recommended for discharge. The most striking difference between this group and the "proved" ulcers was the lower incidence of well-marked periodicity of symptoms—this being noted in only 46%, as against rather more than 75% in the "proved" ulcers. Three patients in this group showed obvious psychological abnormality, and another two had associated "effort syndrome" symptoms.

(2) *Stomach hypertonic, duodenum normal.*—This group of 16 cases presented marked differences in clinical pictures, viewed as a whole, from the "proved ulcers". Definite periodicity of symptoms was noted in only 37%, the pain was in the upper third of the abdomen in only 50%, and vomiting was a leading symptom in 25%. None of these cases was recommended for discharge. Two cases in the group showed obvious psychological abnormality.

(3) *Stomach orthotonic, duodenum normal.*—There were only 5 cases in this group, so that no significant conclusions could be drawn from the study of it. None of them was recommended for discharge; but even with this completely normal radiological picture, a history resembling that regarded as typical of peptic ulcer was found in one case.

(4) *Stomach hypotonic, duodenum spastic.*—There were 13 cases in this group. Viewing them as a group, their histories were not unlike those of the "proved ulcers." There was, however, a much higher proportion of cases in which vomiting was the principal symptom; these amounted to 38% of the total. One case showed evidence of a chronic anxiety state and was discharged on this ground, and one was recommended for discharge on account of the dyspepsia.

(5) *Stomach hypotonic, duodenum normal.*—This group comprised 22 cases. There was well-marked periodicity of symptoms in 59%, the pain was upper abdominal in 64%, with a clear relation to food in 73%. Vomiting was a principal symptom in 23%, and an important secondary one in another 23%. One patient had a recurrent stomatitis accompanying the dyspeptic attacks; 3 showed obvious psychological abnormalities, of whom 2 were recommended for discharge, and a further 4 were recommended for discharge on account of the severity of the dyspepsia.

From this summary survey of a group of cases of dyspepsia with symptoms persistent enough to lead to reference to a medical specialist, certain observations may be made.

(1) Temporary dyspepsias are said to arise and to settle down after "acclimatization" to Army life. There may have been some of these in the 23 "dyspepsias not considered clinically to be organic" and therefore not further investigated; but as no follow-up of these was possible, no useful comment on this question can be made.

(2) A high proportion of the persistent dyspepsias seen in the Army can be shown to be due to peptic ulceration. In the present series, including in the total those "gastro-duodenal" dyspepsias which were not thought clinically to be organic, of 160 dyspepsias for which no organic cause was found outside the stomach and duodenum, 57 or 36% were proved on the strictest criteria to be due to peptic ulceration; and if the 14 cases in which the radiological appearances were suspicious and the diagnosis was justified on additional clinical grounds are added, the percentage of peptic ulcer cases rises to 44%.

(3) Though it may well be that some of the patients in whom no irrefutable radiological evidence of ulceration is found at a single examination may be cases of peptic ulceration, yet it seems likely that among the cases showing a smooth gastric outline and a normal duodenal cap, there are some in whom no ulceration has ever existed. These comprise 43 out of the 137 cases of this series that were X-rayed, that is, 31%. Many of these cases

gave histories compatible with, and some of them highly suggestive of, peptic ulceration. The discrepancy between the results of radiological examination and the conclusions reached on clinical grounds is one of the most difficult problems for the Army medical specialist. Of the 43 cases mentioned showing nothing radiologically suspicious, at least 14 gave clinical histories highly suggestive of ulceration : the converse, an occasional quite nondescript history in a case of proved peptic ulceration has already been noted. The diagnostic problem presented by cases with definite symptoms but no radiological abnormality is a very worrying one: the diagnosis of "gastritis" under which they are frequently placed seems to be one that could only be established in cases of this type by gastroscopy, which is unlikely to be available for more than a very small proportion of such cases, even if it were thought desirable as a routine. And the diagnosis of "duodenitis" seems even less capable of actual proof. On these grounds, the only justifiable diagnosis in these cases, with the investigations generally available, is the non-committal one of "dyspepsia".

(4) In my series, 30% of cases of "proved" ulcer complained of vomiting, but in none of them was it the patient's principal complaint ; but in 17 of the remaining 80 cases, vomiting was the principal symptom. In the hope of detecting some specific effect of an Army régime, these 17 cases were analysed. 10 of them had normal duodenums, pain was generally not prominent, being very slight or absent in 5, a relation of pain to food was detected in only 8, and in none was the pain relieved by food, but the average duration of symptoms in these cases was actually rather longer than in the series as a whole or in the "proved ulcers", being seven years. Any idea that this group represented a separate type of dyspepsia associated with Army conditions was thus eliminated.

(5) The *psychoneurotic element* is very difficult to assess. In only 9 cases was an obvious psychological abnormality, usually an anxiety state, detected. Excluding the cases in which a diagnosis of peptic ulcer was made, this gives an incidence of 9 cases in which psychological factors were detected and regarded as the principal ones in the causation of the symptoms out of 64 "non-ulcer" dyspepsias—that is 14%. Psychological factors seem extraordinarily confusing in dyspeptic cases. Most physicians would agree that they are important in determining breakdown in many instances in cases of peptic ulcer ; but nevertheless no question of making any but an "organic" diagnosis arises in a case of peptic ulcer. It seems not unreasonable to suppose that there exists a gamut of types of case between these predominantly "organic" ones and those in which psychological factors predominate, no organic lesion can be detected and a psychological diagnosis is indicated.

There is no doubt that the atmosphere of uncertainty which tends to surround dyspeptic cases without radiological evidence of ulceration in the Army has a very unfavourable effect on such patients. They tend to drift in and out of reception stations and hospitals without any definite decisions about diagnosis, treatment, and disposal being made. I cannot help feeling that, in a busy general military hospital, decision in these cases must often be made rather arbitrarily, and I must admit to having on several occasions made definite diagnoses on rather insecure grounds in such cases, largely because I have thought that the patients had little chance of improving while overshadowed by this uncertainty. This experience leads me to support the recent suggestion of Sir Arthur Hurst that special units should be established to deal with and make definite decisions about these doubtful cases.

I have been tempted to speculate how far the fixation of the public mind on disorders of digestion by the extensive advertising of proprietary alkaline remedies may have determined that the bodily symptoms of potentially psychoneurotic subjects shall take the form of a dyspepsia. Certainly, some of the advertisements commonly seen for "stomach powders" and the like are masterpieces of reversed psychotherapy, starting from the slight discomfort which anyone may feel after a full meal and skilfully suggesting further alarming symptoms.

My thanks are due to Major J. F. Grant, R.A.M.C., for the radiological data.

Sir Arthur Hurst noted two remarkable differences between ulcers in soldiers and in civilians. The first was in connexion with the relative frequency of gastric and duodenal

ulcer. In civilian private practice duodenal ulcer was about four times as frequent as gastric ulcer, but in hospital practice the incidence was about equal. In spite of the fact that most soldiers came from the hospital class duodenal ulcers were about six times as common as gastric ulcers in the Army. Secondly, from 25 to 50% of civilian patients with ulcers were admitted on account of hæmorrhage compared with under 5% in soldiers. Perforation also appeared to be much less common among soldiers than civilians.

He wondered to what extent medical officers were being misled by relying too implicitly on radiological reports. It was possible that many of the soldiers diagnosed as duodenal ulcer had a scarred duodenum without active ulceration. The presence of a definite niche was the only radiological evidence of active ulceration. It was often extremely difficult to be certain whether a niche representing an ulcer crater was present in a deformed duodenum. In such cases an active ulcer could be diagnosed only in the presence of characteristic symptoms and of occult blood in the stools. For this reason the examination for occult blood after the patient had been sufficiently long on a hæmoglobin- and chlorophyll-free diet was extremely important. A man who had no occult blood in his stools in all probability had no ulcer, as it was present in over 90% of cases when the examination was properly carried out by spectroscopic as well as chemical methods.

In Major Scadding's statistics about 20% of the ulcers were labelled pyloric, although not more than 1% of ulcers were really situated in the pyloric canal. The so-called hypertonic stomach was nothing more than an unusually short, but perfectly normal, stomach, and the "hypotonic" stomach was an equally normal long stomach. The short and long stomachs were variations from the average normal of no more significance than short and long noses.

He had no doubt that Colonel Tidy was right in regarding duodenal ulcer as more common than it was formerly, but some of the increased incidence was apparent and a result of improved methods of diagnosis. The deformity of the bulb in duodenal ulcer was not recognized with the X-rays before 1920, and even the clinical diagnosis dated only from about 1908.

He hoped that when a soldier had work of special importance, which did not prevent him from taking his meals at regular hours and supplementing them with intermediate feeds, it would be possible to keep him in the Army after he had been given strict treatment in bed for a sufficient period to allow the ulcer to heal soundly. He must, of course, be given written instructions how to avoid a recurrence. He wished too that it were possible to come to an arrangement between the Army and civilian hospitals for the continuation of treatment of men with ulcers who were invalided from the Service. They should be encouraged to return as soon as possible to civilian employment, where they would be quite capable of doing a day's work if they lived at home and kept to a proper post-ulcer régime. But before doing so they should remain in hospital sufficiently long for their ulcer to heal.

He was sorry that Colonel Tidy had used the term gastritis to include nervous dyspepsia as well as true gastritis. It should be possible in every case to decide which of the two was present — a matter of great importance — as the treatment of gastritis was quite different from that of nervous dyspepsia. In true gastritis a short period in hospital on strict diet with hydrogen peroxide lavage first thing in the morning resulted in recovery, and in most cases with achlorhydria the secretion of free acid returned. Such cases could always go back to duty, as they differed from ulcer cases in showing much less tendency to recur. It ought also to be possible to get most soldiers with nervous dyspepsia back to duty with the simplest psychotherapy, which should be given by the medical officer in charge of the patient.

Lastly, he believed that the large majority of cases of vomiting in soldiers, whether in association with an organic disease such as ulcer or not, were, as in the last war, hysterical in origin, and simple psychotherapy in the form of explanation and persuasion almost always resulted in the immediate disappearance of the symptom.

Lieut.-Colonel S. J. Hartfall said that true gastritis, which should not be confused with psychogenic, functional, or nervous dyspepsia, could be diagnosed gastroscopically. There were cases in which it was difficult to be positive, but sometimes it was very

important to be able to say that there was nothing abnormal on inspection in a given stomach, and among the cases which he had gastroscoped a negative finding came out very frequently.

In accounting for dyspepsia in the Army his own incidence was 40 to 60% of ulcers, and the figures of Newman and Payne were coming down to somewhere about the 60% level. But Major Scadding in his paper was getting back to something like Newman and Payne's original figures of 90% for peptic ulcer. Whether the explanation of that was that his neurotics had been filtered off he did not know. Though he found cases of psychogenic dyspepsia coming along, which he investigated, organic cases also came along, and it was on that type of case that his figures were based.

The incidence of neurotic disease among his dyspeptics at the present time was about 60%. That did not mean that they were all neurotic dyspepsias. By that he meant that there was quite a sprinkling of cases with ulcer or which had had it, together with manifest neurotic symptoms; but in about 60% of cases there was a fundamental neurotic basis present.

He had investigated 89 cases of dyspepsia with negative investigations for organic disease by X-rays, occult blood, and test meal. It was thought that a high proportion of gastritis might be found among them. These were the *prima facie* neurotics. One gastroscoped them, and 60% of them were entirely negative, and so with every other investigation. The gastroscopy being negative, one could hand them over to the psychiatrist. Of this group 20% had a superficial patchy gastritis, sometimes fairly diffuse, but not very serious. His own treatment for these superficial cases was to keep the patient in bed for ten days to a fortnight, and to give every morning a gastric lavage with hydrogen peroxide, one drachm to the pint, followed immediately by two drachms of an aluminium preparation, and continuing with a teaspoonful of that preparation four-hourly, interspersed between each meal throughout the day, with a light diet and omission of tobacco. The cases improved very rapidly, and could be got back quickly. As to the final 15 or 20%, the positive findings by the gastroscope were these: acute gastric ulcer missed by X-rays, 4%; chronic gastritis with rather severe patchy atrophic or hypertrophic change, 10%,; anastomotic gastritis, 2%. Among these negative dyspeptics it must not be thought that the explanation was going to be found in a non-suspected chronic gastritis in any very large proportion. It would be evident here and there, but not in many cases.

Mr. Reginald Payne said that everybody was agreed about the magnitude of the dyspepsia problem as it occurred in France and in this country, and as it was still occurring. However, the problem was a changing one, and the cases that Dr. Newman and he saw in the early part of last year were very different from those being seen now.

One point elicited was the very early age-incidence of some of the duodenal ulcer cases. Some of them dated from the ages of 10 to 15, and the peak occurred between the ages of 20 and 25. Another clinical point was the frequency and importance of vomiting as a paramount symptom. These men did not go sick until they were vomiting profusely most of the day. Again, as an important finding in the ulcer cases, weight loss was extremely marked. In the cases from France the average weight on mobilization was 148 pounds, and the average weight loss was 12·1 pounds. The weight of the men who broke down in England was on mobilization 149 pounds, and the average weight loss 5·7 pounds. A study of the dental aspect showed that 37% had inadequate teeth for chewing, either with or without dentures. Another point was that approximately 15% of the men seen in the early days of the war had got into the Army with abdominal scars betraying some antecedent serious gastroduodenal operation.

On the basis of the investigation they made certain recommendations with regard to the recruiting, disposal, and treatment of these cases. They considered it worth while that valuable men should always be retained if a suitable dietetic regime could be found. Colonel Tidy had stressed the magnitude of the problem, and the fact that about 50% of cases of dyspepsia were organic. Rather similar findings had been reported by Morris and others.

At the time of the investigation there were very few malingerers. At some hospitals they were told that the presence of psychologists in the Army produced dyspeptics. They

did not believe that, but in many cases it was obvious that investigation had failed to establish an exact diagnosis. It was very important to arrive at an accurate diagnosis in all cases as early as possible. Unless there were accurate histories most of the other investigations would be wasted. The difficult or doubtful or prolonged case must be investigated by all the means at their disposal. Finally, some one individual must be in a position to summarize the evidence. The diagnosis should not be left to the radiologist alone or indeed to any one who had not had the benefit of all the data.

Gastroscopy would not help in all cases, but it would play a part in solving that very big group of what Colonel Tidy had called "gastritis". The word "gastritis" would hardly apply to so large a group of cases (35%). At the Post-Graduate Medical School they found a considerable number of cases of gross organic disease that gastroscopy would help to elucidate, either by positive or by negative findings. In the cases they investigated very few of the men should have got into the Army at all and they would not have passed a life insurance examination. They were only nuisances in the Army, but they were useful as civilian workers.

Therefore he made a plea for the most accurate diagnosis possible of these gastro-duodenal cases. A mass attack upon them would lead to errors, and it was an individual approach that would solve the problem.

Colonel E. B. Marsh spoke as a regular Army physician, one who had been practising medicine in the British Army in various parts of the world since the beginning of the last war. The main thing to decide on seeing the soldier was: "Is this man fit for service as a soldier?" If so, in what category was he to be placed? This was particularly important in the middle of a war, because, unless one decided at once and quickly by a careful taking of the history and examination of the case, waste of time would be inevitable.

There was nothing that Colonel Tidy had said with which an ordinary practising physician in the Army could disagree. He himself, a member of this small band—after qualifying as an Army medical specialist—was posted to Aldershot, and was at once struck with the fact that the age-incidence for the onset of ulcer was between 19 and 22, while the books of those days said that it was between 30 and 35. This was because in the Army they saw their cases at the onset of the first symptoms, whereas in civil life patients went into large hospitals for investigation only after they had been dealt with by practitioners for a number of years.

It had been his practice not to use the term "gastritis", which had come in for a good deal of discussion, unless it was thought on clinical grounds that the case was one of true gastritis. He used to call the sufferers from gastritis either "beer-drinkers" or "bun-eaters". In the old Army days, the "beer-drinkers" were the larger group, but in later years it was the "bun-eaters". "Soldier's stomach" he had never heard of, either before the war or since; it was not an Army term.

Many first-class physicians in the Army to-day could be trusted to carry out the diagnosis, without making a general issue of gastroscopes. With experience and careful examination it ought to be possible to decide whether a man was fit for duty in the Army or not.

In the North-West of India the young British soldier rarely developed ulcer, either gastric or duodenal. In five years' experience there he did not see more than two cases of ulcer, whereas in England among the same men he had seen a large number. The average age of soldiers in India was perhaps a little higher (20 to 23).

Another interesting point was that in certain countries, for instance, India and Egypt, if the fractional test meals were examined in a hundred healthy young soldiers, it would be found that the total acidity and the free acidity were lower than in Ryle's figures.

Colonel Tidy (in reply) said that duodenal ulcer was certainly far commoner than gastric ulcer in the Army. This was also the general experience in private practice. On looking up reports at St. Thomas's Hospital for a recent year he found that more cases of gastric ulcer were admitted than duodenal. There must be some special reason for this, possibly

the greater severity of gastric ulcer. He agreed that "gastritis" was not a good term, but no satisfactory alternative had been suggested. He did not agree that a negative gastroscopic examination was sufficient evidence to regard cases in this group as psychoneurotic. He objected to the term " soldier's stomach ". Cases which were sent to hospital time after time developed a condition not unfairly described as " hospital stomach " but not as " soldier's stomach ".

Section of Odontology

President—EVELYN SPRAWSON, M.C., D.Sc., L.R.C.P., M.R.C.S., L.D.S.

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Benign Neoplasia of Tooth and Bone

By E. WILFRED FISH, M.D., D.D.Sc., D.Sc.

(*From the Meyerstein Laboratory for Dental Research, St. Mary's Hospital, Paddington, London, W.*2).

INTRODUCTION

THIS communication consists of a record of a rare and apparently neoplastic lesion of the dental pulp and of a series of cases exhibiting a similarly destructive lesion originating in the parodontal membrane. These conditions correspond so closely to recognized but inconclusively classified bone lesions that an attempt is made to compare the two series in order to elucidate the essential pathology of both.

The problem of classifying benign tumours which arise in tissues derived from the mesenchyme is complicated by the fact that it is in these particular tissues that the massive cell proliferations of inflammation take place.

In the case of the calcified connective tissue there is the further complication that whenever an osteoblast is produced it deposits some matrix, and whenever an osteoclast is produced it eats away the matrix in its vicinity whether it be new or old. Moreover no tumour of any sort can occur inside a bone without osteoclasts making room for it: indeed if the undifferentiated cells of the bone are sufficiently irritated, osteoblasts and osteoclasts will in any case appear so that if the source of irritation has been overlooked they may be regarded as neoplastic, or if another tumour is causing irritation they may be mistaken for a part of that tumour.

A detailed study of inflammatory reactions in bone and the dental pulp does, however, lead to the exclusion of certain morbid conditions from the category of inflammatory phenomena and indicates that they are neoplastic in nature. Moreover, when these exceptions are assembled they form a remarkably symmetrical series, the bone lesions corresponding to the tooth lesions and each fulfilling the theoretical prediction of neoplasia in the tissue concerned.

If, however, one is unwilling to regard the bone lesions as neoplastic it is still of interest to observe the parallel series of tooth lesions which would then also of course await precise classification.

The tooth lesions.—It has been the usual practice to group together all tumours of the dental tissues as odontomes. The only truly neoplastic members of the group, however, that is, tumours in which uncontrolled cell proliferation takes place without any typical

termination, are the adamantinoma and the cementoma. The rest of the odontomes are developmental tumours arising from aberrations of growth but not exhibiting true neoplasia.

In the composite odontomes, representing a missing tooth, growth is self-limiting; they cease to grow at about the time when the tooth which they represent would have been completed. They may therefore be compared with congenital abnormalities of other organs, as for example, congenital cystic kidney; the cells have failed to inherit in full their usual instinct for design which normal cells exhibit even in tissue culture.

> A girl whose father had a normal dentition but whose mother's upper lateral incisors were congenitally absent, was found to have one normal lateral incisor while the other was represented by a composite odontome (fig. 4 (*a*)). Another girl with a similar heredity produced a normal right upper lateral and no left upper lateral at all.

The dental and dentigerous cysts arise from epithelial remnants and may perhaps be classified with the inclusion dermoids. As in the case of inclusion dermoids, there is often a history of irritation to the cell remnants from which they arise, and like the dermoids, both dental and dentigerous cysts cease to grow, and indeed undergo involution if they are marsupialized, that is, opened to the surface and kept open so that internal tension is abolished. Their constituent cells are therefore not essentially neoplastic.

The rare fibrous odontome appears to be a fibroma of the periodontal membrane or a rickety hyperplasia of the tooth sac. It therefore comes to include an unerupted tooth or the roots of one which has erupted. It may perhaps be a close enough neighbour to be regarded as a tumour of dental origin though of course it is not formed of calcified tissue.

Of the two odontomes which are left the adamantinoma will not be included in the present series because it is an epithelial tumour and so could have no counterpart in bone neoplasia. Moreover it is not a neoplasm of the mature organ but of the tooth bud and so holds an almost unique position in the body. The cementoma is, however, a benign tumour of the mature tooth composed of calcified connective tissue and must therefore be considered and included.

The other two morbid conditions which it will be suggested may represent neoplastic change in the cells associated with a mature tooth have not generally been regarded as neoplastic; one has been called "inostosis" and the other, if it has been observed at all, has been included in the group of cases indicated by the descriptive title of "pink spot". The specimens to be described, however, appear to the author to be examples of true neoplasia and in any case shed considerable light on the nature of corresponding lesions in bone which may be of some help in classification.

The bone lesions.—Amongst those lesions which may be regarded as benign tumours of bone, there is also included a developmental abnormality quite comparable with the composite odontome. It consists of an abnormal bony excrescence at the epiphysial line, cartilage capped, which like the odontome ceases to grow when the bone reaches its full development. Apart from this there are the comparatively rare benign endosteomata, the ordinary ivory exostoses, bony epulides, osteoclastomata and an ill-defined group of lesions called localized or focal osteitis fibrosa.

Tooth and bone lesions compared.—If the neoplastic nature of all these lesions be for the moment assumed and appropriate synthetic names are assigned, they form, as already observed, a very symmetrical series:

Bone tumours	Tooth tumours
Endosteoma (including some examples of local osteitis fibrosa)	Endodontoma (certain cases of pink spot)
Periosteoma (ivory exostosis and fibrous epulis containing bone)	Parodontoma (cementoma)
Osteoclastoma (myeloma)	Odontoclastoma (inostosis)

Identification and definition of bone lesions.—Unfortunately there is in addition to the problem of classification an equally confusing problem of identification and definition. Focal or local osteitis fibrosa is a diagnosis which can only be applied when histological evidence is controlled by clinical and radiological examination, since many other conditions present the same histological picture. Not only generalized osteitis fibrosa or an early case of Paget's disease but any fairly severe irritant will produce a histological picture

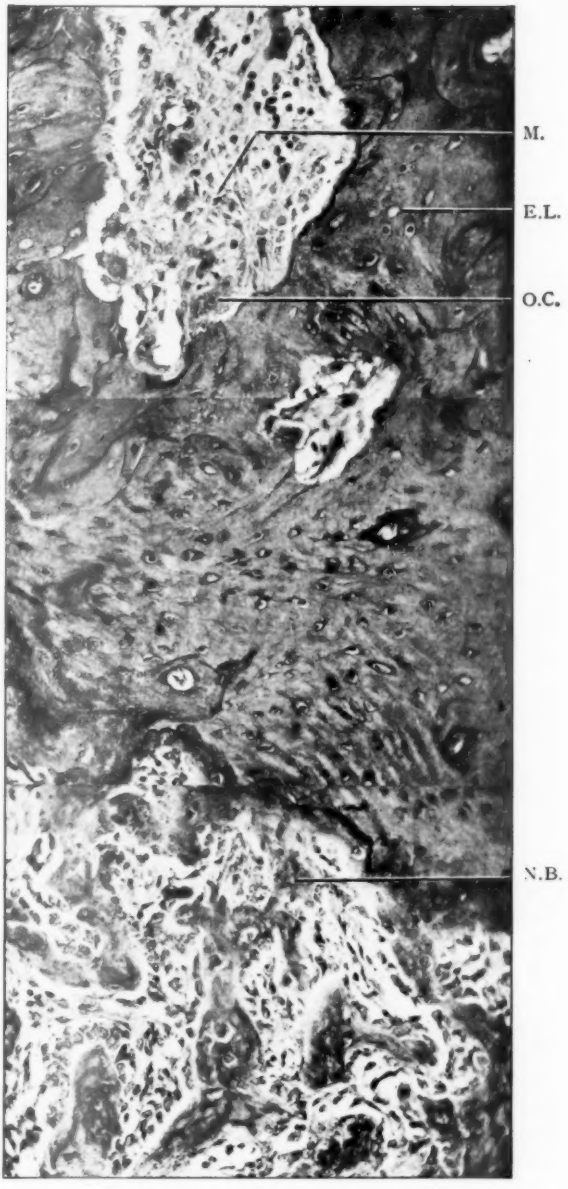


FIG. 1.—Photomicrograph × 190 of symphysis menti of guinea-pig to show the effect of implanting thymol in the bone at a point "north" of the part of the section illustrated. The animal was killed forty-eight hours after implantation. Undifferentiated cells are undergoing mitosis at (M.). Osteoclasts (O.C.) have been produced and bone is absorbing in the part nearer the irritant. Osteoblasts have appeared and are building new bone (N.B.) at the more distant point where the irritant is weaker. The osteocytes have disappeared or are pyknotic at (E.L.) and have survived further away from the irritant.

which could quite easily be mistaken for focal osteitis fibrosa in certain parts of the field. For example, fig. 1 shows the result of the experimental implantation of a pellet of wax impregnated with thymol into the bone of a guinea-pig. Osteoclasts, osteoblasts and fibroblasts are all active but their activities are more orderly than in osteitis fibrosa.

This confusion is particularly liable to occur in the jaw when an indefinite patch of alternating rarefaction and sclerosis of the alveolar bone is observed in the skiagram. A diagnosis of focal osteitis fibrosa may even be confirmed by a histological section prepared from a small fragment of the alveolar crest, which shows a few osteoclasts, some increase in fibrous tissue and abnormal activity of osteoblasts ; but both the radiological and histological findings may quite reasonably be attributed to nothing more than the response of the bone cells to a widespread diffusion of tissue breakdown products from a chronic ulcerative marginal gingivitis, indicated histologically by the presence of a diffuse cellular infiltration of the bone.

Conversely, the sharply defined lesion in fig. 2 which had been diagnosed as focal osteitis fibrosa on the histological findings (fig. 3) was not associated with any form of irritation so far as could be observed nor was there any infiltration of the tissues by inflammatory cells. From its circumscribed appearance, its continued growth at the expense of the normal tissues and from its failure to serve any useful purpose or progress towards any typical termination, it might well be regarded as neoplastic.

In order if possible to escape this source of confusion therefore, the first group of endosteal lesions in the classification, to which the term endosteoma is applied, may be taken to include, at any rate for the moment, only those sharply defined solid growths in the ends of the long bones or in the lower jaw which are called indifferently either focal osteitis fibrosa or endosteomata, and would exclude the indefinite patchy lesions frequently seen in skiagrams of the jaws which may be much more correctly ascribed to toxic irritation. These latter are not progressive.

Identification and definition of tooth lesions.—A similar ambiguity exists in the use of the old-fashioned term " pink spot ". This may even be applied to an absorbing temporary tooth in which the osteoclasts have reached and perhaps invaded the enamel before being killed by sepsis from the parodontal sulcus. There are also many examples of absorption of dentine by osteoclasts in cases of chronic infection of the pulp. Almost every case of polypus of the pulp shows this (Dolamore, 1923) and sometimes quite extensive absorption of dentine and deposition of calcified repair tissue is to be seen in cases of chronic pulp abscess (Fish, 1939*a*).

Another instance of absorption of the dentine which may produce a pink spot and must not be confused with the lesion about to be described as an endodontoma, is to be observed in teeth which have a history of receiving a blow some years before and of having turned grey. The sequence of events appears to be initiated by infarction of the pulp following rupture of its efferent vessels. The pulp thus becomes stuffed with blood through an afferent vessel and if removed at once looks, macroscopically, like a firm blood-clot. The dentine is suffused with and discoloured by hæmolysed blood pigment. If the pulp is left in situ most of the cells degenerate including the odontoblasts (fig. 7(*a*)) so that the dentinal tubules contain only the disintegrating fibrils. The massive collagen deposits in the pulp itself which follow the degeneration of the fibroblasts undergo a hyalin change and both calcific degeneration and fat replacement occur (Fish, 1938*a*). The disintegrating fibrils in the dentine provide a constant irritant to any undifferentiated cells which may survive in the pulp, so that osteoclasts may be produced and the dentine absorbed (figs. 4 (*h*) and 7 (*b*)).

Unfortunately it is not always possible to determine to which category the previously recorded cases of pink spot belong, and quite often cases of dentine absorption arising from the parodontal membrane, that is, inostosis, have been included as well. The classical description by Mummery in *The British Dental Journals* of 1920 and 1926 is perhaps the most complete. In the former paper he reviews and illustrates cases in which cells from the pulp have excavated the dentine and in which there is no abnormal communication with the parodontal membrane. The teeth concerned were free from caries. In the later paper he is quite clearly including cases where a lesion, destroying the dentine of a tooth, has taken origin from the parodontal membrane and involved the pulp only secondarily. It would seem both desirable and important to separate these two types and to exclude infarction though Mummery does not do so. In the present paper they are called " endodontoma " and "odontoclastoma " respectively.

Unfortunately in almost all cases the new growth, whether of pulp, tissue or parodontal membrane, reaches the surface and becomes infected. This circumstance, together with the fact that dentine absorption and the deposition of calcified tissue of repair are both regular features of chronic pulpitis, led Mummery to regard his cases of pink spot and inostosis as chronic perforating hyperplasia of the pulp and he was evidently impressed by the constant presence of inflammatory cells. The inflammation is, however, absent in a number of specimens in the present series, and where it occurs is clearly secondary to external contamination.

The endodontoma and the endosteoma.—The lesion to be described as an endodontoma (figs. 4 (*b*), 5 and 6) was first observed incidentally in the skiagram (fig. 4 (*b*)) which corresponds closely to a case briefly recorded by Parker (1929). A similar case was recorded by Pritchard (1931). Clinically there were no symptoms; there was an amalgam filling in good order on the distal aspect of the crown and a small spot of new caries, clinically invisible, on the mesial aspect. The patient was a woman 26 years old and the other teeth were normal. The affected tooth was the left lower first premolar. Histologically the dentine had been and was being very extensively absorbed from the pulp surface in the middle and upper third of the tooth although there is normal pulp tissue with its usual odontoblast layer both at the coronal and apical ends. Nevertheless osteoclasts have burrowed into the dentine and were still continuing to do so when the tooth was extracted (fig. 6 (*d*)). In many places the lost dentine had been replaced with a primitive type of coarse fibre bone, histologically indistinguishable from the bone of the endosteoma or that of an exostosis or even lacunar cementum or any calcified tissue of repair, all of which have a close resemblance to each other and have been previously discussed (Fish, 1939*b*). Not only is this calcified osseous tissue deposited in the Howship's lacunæ of the absorbed dentine but there are a great many free masses of it in the soft tissue of the enlarged pulp chamber.

No significance is attached to this feature in earlier descriptions and it seems doubtful whether it can have been so pronounced in Mummery's specimens. It is nevertheless of some importance, for a typical field of the new growth in the enlarged pulp chamber does not resemble normal pulp tissue at all or even inflamed pulp but is identical with the histological appearance of an endosteoma (fig. 3) or a patch of osteitis fibrosa in bone. There are osteoblasts [*sic*] building the new deposits of primitive bone and osteoclasts eating it away again, as well as tunnelling into the dentine walls of the cavity; a certain amount of fibrous tissue is present and there are innumerable undifferentiated cells or primitive fibroblasts which are definitely more embryonic in type and in a more active phase than the corresponding cells of the normal pulp remnant (fig. 6 (*b*)).

At one point the tumour had almost reached the surface of the enamel at which moment it must have shown as a pink spot. The phase changed, however, and deposition set in, repairing the lesion. Since then caries developed and opened into the repair tissue; it actually caused a small chronic abscess at one point in the growth; but obviously the inception of caries must have been a sequel to the deposition of the new osseous tissue, since it is the new tissue itself which has become carious. Moreover, carious dentine cannot be absorbed any more than an infected sequestrum of bone since its toxic content would kill the osteoclasts (Fish 1939*a*).

The pulp lesion was therefore present before the caries or the abscess and was not a result of irritation from them. It may also be observed that the dead tract under the filled cavity on the other side of the tooth was perfectly sealed off from the pulp and the soft tissue below the secondary dentine showed no sign of irritation nor did it take part in the lesion.

Apart, however, from the fact that the abscess is in the growth and not in a part of the original pulp chamber, the lesion bears no resemblance to the ordered reaction of pulp tissue to septic irritation which can readily be described in concentric zones of reaction (Fish, 1939*a*). Osteoclasts are burrowing in the utmost recesses of the dentine (figs. 5 and 6 (*d*)) far removed from any possible toxic irritation and osteoclasts and osteoblasts are also completely mixed up elsewhere in the lesion, one destroying what the other produces; they are not arranged in the orderly and purposeful way which is typical of the response to irritation (fig. 1).

At one point the growth has reached the parodontal membrane but the opening was extremely small, as verified by serial sections of which fig. 5 shows its greatest diameter.

FIG. 2.—Skiagram of an endosteoma of the mandible (by Dr. Courtney Gage).

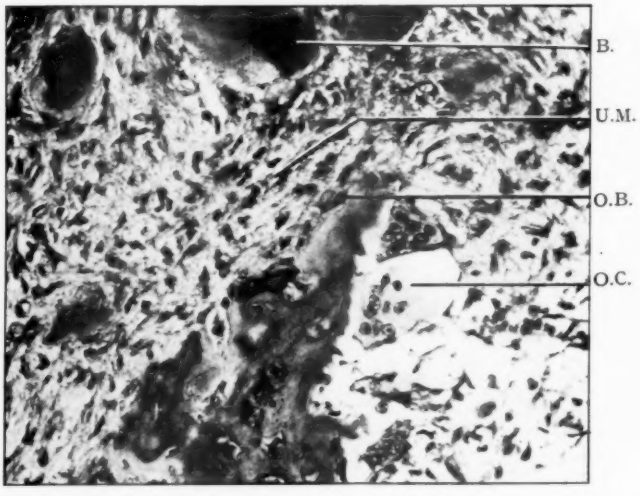
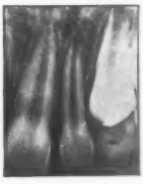


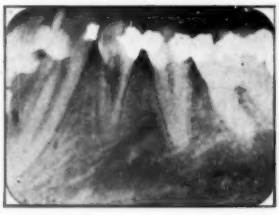
FIG. 3.—Photomicrograph ×250 of a section of the tumour shown in fig. 2 (removed by Mr. Handfield-Jones). (O.C.) osteoclasts, (O.B.) osteoblasts, (U.M.) undifferentiated mesenchyme cells, (B.) coarse fibre bone.

FIG. 4.—(*a*) Odontome (*see* text) from child aged 10 years. (*b*) Endodontoma (*see* text). (*c*) Cementoma. The other teeth were radiographically normal. (*d*) Osteoclastoma between the canine and first premolar. The edge of the bone below the tumour is well defined. Tumour removed and both teeth retained. No recurrence in two years. (*e*) Odontoclastoma (*see* text). (*f*) Odontoclastoma; (i) taken ten months before (ii). In (i) the roots are normal, in (ii) there is a granuloma on $\underline{2}|$ and an odontoclastoma associated with $\underline{1}|$. (*g*) Odontoclastoma; (i) was taken two and a half years before (ii) (*see* text). (*h*) Absorption of the dentine following infarction of the pulp as the result of a blow ten years before (cp. fig. 7). (*i*) Bony epulis arising from labial alveolus of $\overline{3}$.

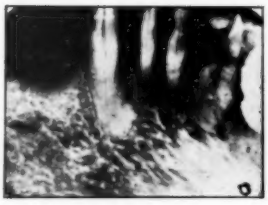
(*See opposite*).

(*a*)





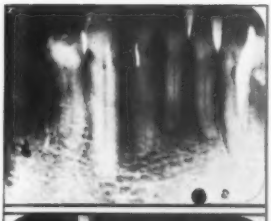
(*b*)

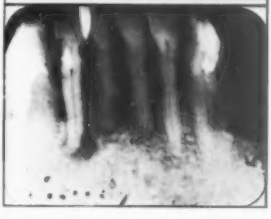


(*c*)

g (i)

(*h*)





f (i) and (ii)

g (ii)

(*i*)

(*d*)

(*e*)

FIG. 4 (*a-i*).

It is possible, however, that the growth could have originated from the parodontal membrane though the skiagram shows no sign of disturbance at this point, and the arrangement of the fibrous tissue at the opening suggests a reaction by a normal periodontal membrane against intrusion by the growth. Histologically also, there is much more deposition of new calcified matrix in the growth than in any of the lesions known to have taken origin from the parodontal membrane. Nevertheless the possibility of a parodontal origin exists and it is most important to collect cases, if they exist, where it can be excluded with certainty.

The endosteoma shown in figs. 2 and 3 has precisely the same histological features as the endodontoma. The same meaningless absorption and deposition of matrix are seen, followed by renewed absorption. There are numerous undifferentiated cells and fibroblasts associated with the continual production of fibrous tissue. This lesion had persisted for eight years without achieving any purpose. The cortical bone of the jaw had shared the fate of the cancellous interior, while in places the periosteum had deposited a thin layer of new bone as a reaction to the irritation of the growth. There was no apparent cause; the woman, who was 32 years old, was otherwise healthy and the teeth in and around the tumour showed no gross signs of parodontal infection, nor did they become involved by the growth.

The periosteoma and the parodontoma.—The next pair to be considered are the ivory exostosis and the cementoma or cementome which are called "periosteoma" and "parodontoma" respectively in the suggested classification. It is clear that since the ivory exostosis is a proliferative lesion on the surface of bone there is no need for any bone absorption to make room for the neoplasm and therefore no need for osteoclasts; in any case, none ever appear. The slowness of growth in the lesion may be accounted for by the nature of its cells for they nearly all differentiate and produce bone matrix though they do not fashion a true Haversian pattern in it (Fish, 1939*b*).

Since the cells do produce matrix, however, they become enclosed within it, and can then neither proliferate even if that were otherwise possible, nor can they produce more matrix though they can and often do die (*ibid.*). The result is that only the few remaining cells at the surface, which do not differentiate, can take part in the neoplastic process.

The same observations are applicable to the cementoma of which some truly enormous examples measuring, in the horse, as much as $10 \times 6 \times 8$ inches are recorded (Gabell, James and Payne, 1914). In the case of the cementoma there is an appropriate absorption of bone to accommodate the tumour (fig. 4 (*c*)), but this takes place in a slow, orderly manner, and being purposeful is clearly not a part of the neoplastic process which is itself again without apparent purpose, cause, control or typical termination.

There are examples in the case of both the cementoma and the ivory exostosis of multiple lesions, but multiple cementosis of the teeth does not proceed to the production of such large masses of cementum as does the true cementoma which, even in man, may weigh over 11 grm. (*ibid.*). There are, moreover, histological differences; for example the multiple lesions are relatively avascular and the new tissue is deposited in layers. The cells in the deeper layers are dead, suggesting that the reaction may be a hypersensitive response to toxic absorption from the gingival trough or to some poison circulating in the blood. In one of the author's cases multiple cementosis was associated with Heberden's nodes on the phalanges of the fingers.

The essential pathology of the multiple lesions seems to be allied to that of the bony bridges in spondylitis and the osteophytes of osteoarthritis, and while it is correspondingly obscure, all these arthritic lesions do appear to be a response to irritation and are associated with inflammatory infiltration. They bear only a superficial resemblance to true neoplasia.

In the true cementoma there are blood-vessels, the surface of the growth is irregular, and the matrix is not deposited in obvious layers, nor is it arranged symmetrically around the root of the tooth.

In addition to the ivory exostosis, which is, of course, by no means universally regarded as neoplastic, though no alternative explanation seems to have been offered, there is a modification of the ordinary fibrous epulis (fig. 4 (*i*)). Most fibrous epulides contain spicules of bone, but the present example, situated on the buccal gum margin of the right lower canine of a woman of 30, consisted entirely of bone under the mucoperiosteum, and was firmly attached to the alveolus by a bony pedicle. Springing from the parodontal

FIG. 5.—Photomicrograph × 10 of endodontoma (*see* text and fig. 4 (*b*)).

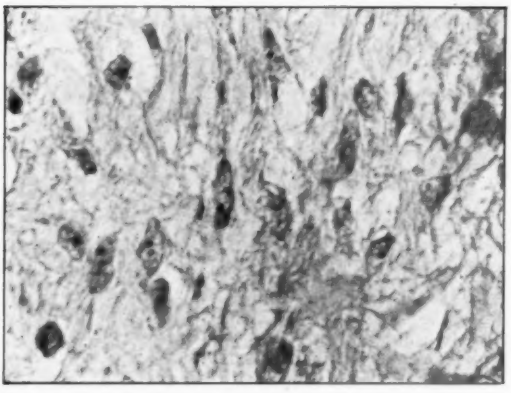


FIG. 6 (*b*).

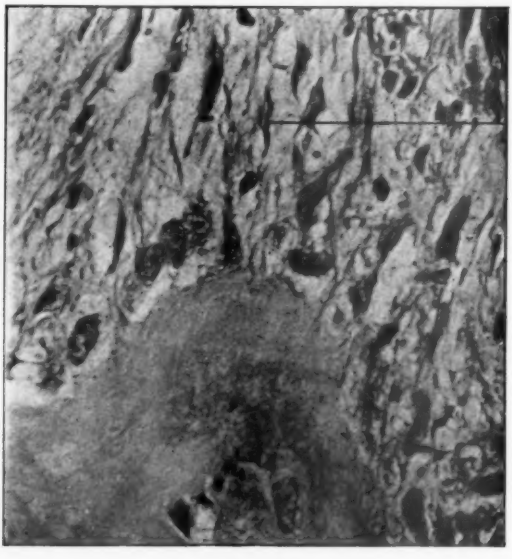


FIG. 6 (*c*).

FIG. 6.—(*a*) Photomicrograph × 280. Osteoclasts (O.C.), osteoblasts (O.B.) and undifferentiated cells (U.) from endodontoma in fig. 5. The patch of new primitive bone is being absorbed (cp. fig. 3). (D.) = dentine. (*b*) Photomicrograph × 660. Undifferentiated cells ; the proliferating cell of the lesion. (*c*) Photomicrograph × 660 showing these cells differentiating into primitive osteoblasts and fibroblasts. (*d*) Photomicrograph × 230. Another part of the lesion showing osteoclasts tunnelling into the dentine.

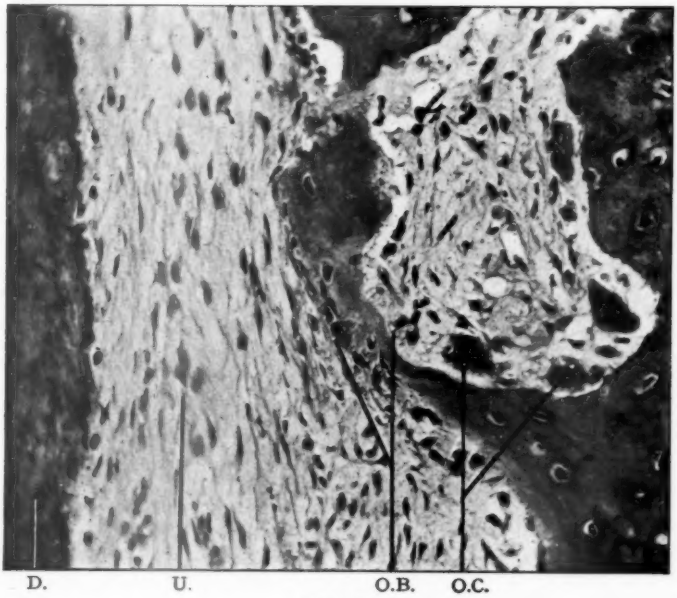


FIG. 6 (*a*).

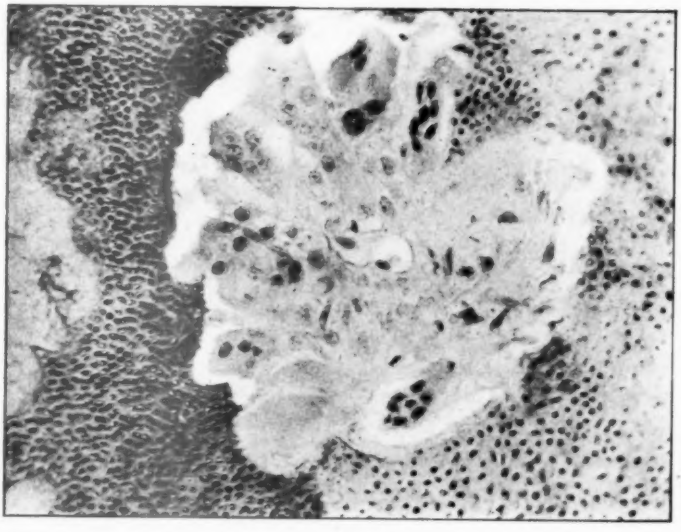
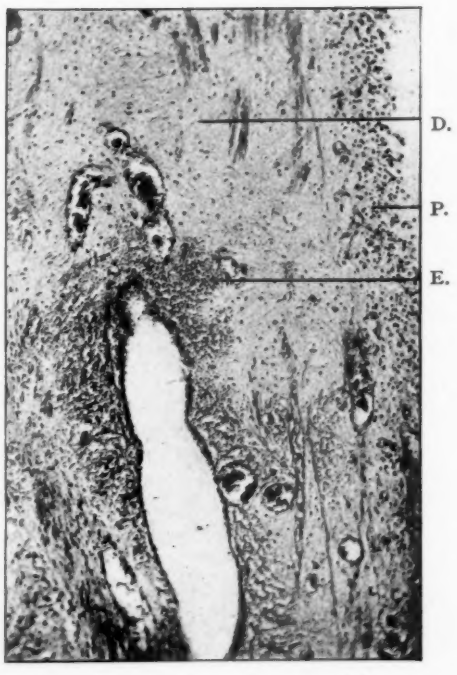


FIG. 6 (*d*).



(*a*)

(*b*)

FIG. 7.—(*a*) Photomicrograph × 75 of part of the pulp of a human incisor which received a blow four days before extraction, causing infarction of the pulp. (E.) = extravasated blood. (D.) = degenerated pulp tissue with pyknotic odontoblasts (P.) (*b*) Photomicrograph × 8 of a human upper central incisor which received a blow twelve years before extraction and suffered infarction of the pulp (cp. fig. 4 (*h*) and *see* text). (F.) = Fibrous degeneration. (R.) = Fat replacement. (H.) = Hyaline degeneration. (C.) = Calcific degeneration.

membrane and the alveolar bone this almost isolated marble of osseous tissue seems to form a link between the ivory exostosis and the cementoma, both of which it resembled histologically and genetically, but with neither of which could it be entirely identified.

The osteoclastoma and the odontoclastoma.—There remain to be described the two examples of destructive tumour, the osteoclastoma and the odontoclastoma or "inostosis". The osteoclastoma or myeloid epulis of the lower jaw is often differentiated from that of the ends of the long bones or of the vertebral column because the latter are endosteal, while the former is regarded as a surface lesion. In the ends of the long bones the tumour appears radiographically as a collection of bubbles, and there is a condensed peripheral layer of bone deposited by the periosteum. This is absent in the jaw, and the skiagram simply shows a deficiency of bone (fig. 4 (*d*)). Nevertheless, it still may be the case that the myeloid epulis of the jaw also starts endosteally in the alveolar bone, but rapidly appears on the surface because the mucoperiosteum is generally ulcerated between the teeth and has lost its osteogenetic character. It does not therefore react and deposit the condensed peripheral layer.

Histologically the tumours are indistinguishable from whichever situation they are taken, and though in some there may be more spindle cells of the fibroblast type and in others more round cells, the typical cell in all is the multinucleated osteoclast. It is not unusual to find the outline of the cytoplasm so indefinite in some of these giant cells as to suggest fusion of separate osteoclasts (Fish, 1938*b*).

The corresponding tooth lesion "inostosis", or "odontoclastoma", as it may prove to be, is by no means uncommon. Many of Mummery's cases of pink spot were of this type, and in the discussion of a paper by Fothergill in 1900, Lloyd Williams, Baldwin and Badcock all quoted cases. Pritchard (1939) described a number of cases, and the present series could have been extended if space had allowed (fig. 8). The condition may develop in any of the teeth, incisors, canines, premolars or molars indifferently, and all the cases illustrated occurred in fully erupted functional teeth of adults, though the same lesion is reported in impacted unerupted teeth.

The essential lesion is a loss of tooth substance brought about by osteoclasts or "odontoclasts" tunnelling into the cementum and dentine from the parodontal membrane. The cells may reach and invade the pulp, though they tend to avoid it and burrow along parallel with its surface, appearing again on the opposite side of the section having passed right round the pulp chamber in the dentine.

The odontoclasts may also extend the lesion towards the neck of the tooth until it invades the parodontal sulcus, and it is generally this incident which calls attention to the condition. Up to this point the lesion is painless, but at any moment after it has approached the sulcus an accidental tear may expose the growth and acute infection may supervene with pain, which may have the symptoms of both acute parodontitis and acute pulpitis since the pulp may be involved by direct spread. Conversely, exposure of the growth may merely be followed by chronic ulceration of its minute surface, where it encroaches on the sulcus and where its tunnelling may sometimes be discovered incidentally with a probe.

Extension of the tumour may also take place in a third direction, as shown in fig. 4 (*e*, *f* and *g*). The example in fig. 4 (*e*) occurred in a woman aged about 60, and shows considerable absorption of the substance of the tooth with a fairly wide extension into the bone. It is significant that while an osteoclastoma never attacks a tooth (fig. 4 (*d*)) an odontoclastoma often attacks bone (fig. 4 (*e*, *f* and g)). It is equally remarkable that whereas in the osteoclastoma of jaw there is no reactionary *lamina dura* of newly deposited bone round the growth, when an odontoclastoma invades bone there may be evidence of such a layer (fig. 4 (*e* and *f*)), though it does not always appear (fig. 4 (*g*)).

Histologically the growth, as observed in the depths of the dentine (figs. 9 and 10), consists of undifferentiated mesenchyme cells in a delicate reticulum with numerous odontoclasts lying in the Howship's lacunæ they have made. In other parts there are fully differentiated cells having the appearance of osteoblasts which are seen to be depositing new calcified tissue on the surface of the dentine in such Howship's lacunæ as have been deserted by the odontoclasts (fig. 9). The new tissue is the same primitive bone as that observed in the endodontoma, endosteoma or any other bone or tooth tumour, and as in these other tumours it is constantly being absorbed and replaced again (fig. 10).

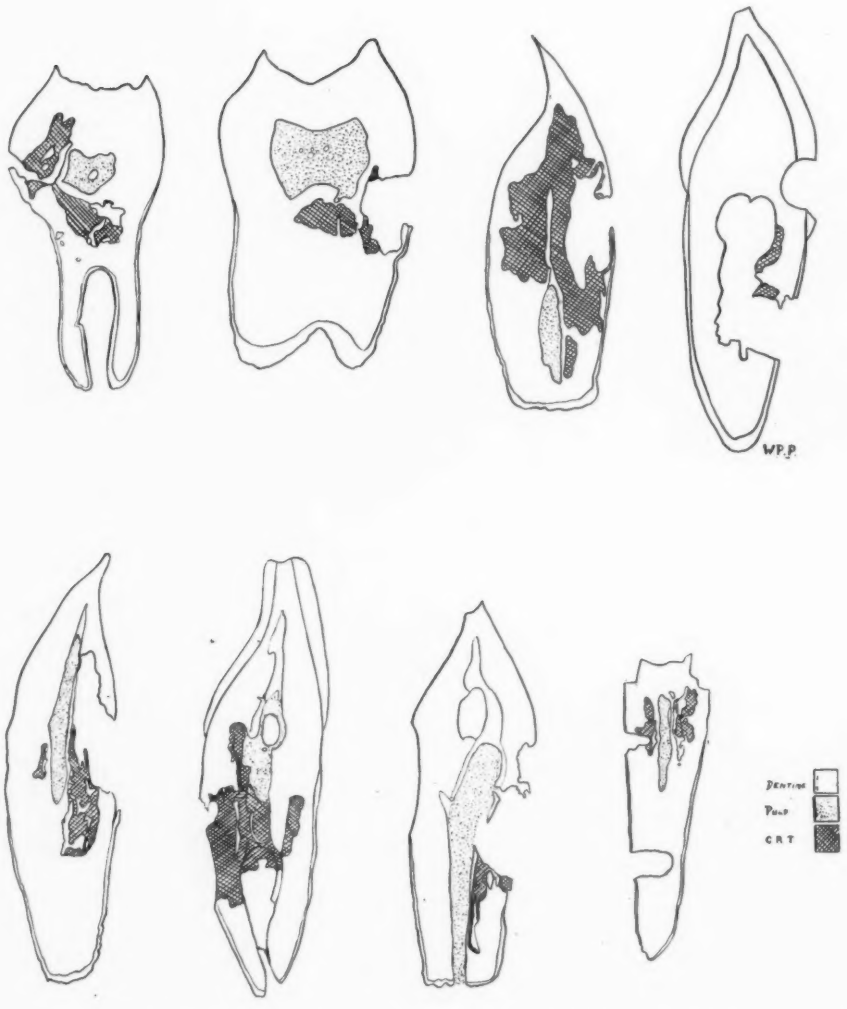


FIG. 8.—Tracings from eight specimens of odontoclastoma to show the extent of the lesion. Pulp tissue is stippled and calcified replacement tissue is cross-hatched.

FIG. 9.—Photomicrograph × 250 of part of the calcified replacement tissue of an odontoclastoma with islets of undifferentiated cells, osteoclasts (O.C.) and primitive osteoblasts (O.B.). (D.) = dentine.

FIG. 10.—Photomicrograph × 135 to show the irregularity of the attack on the dentine in an odontoclastoma; it is precisely similar in the endodontoma. (D.) = dentine and (B.) = calcified replacement tissue.

There is, however, one feature in the general structure of the growth which serves to distinguish it from the endodontoma, and that is that there are not so many independent masses of this new bone lying free in the soft tissue of the odontoclastoma as there are in that of the endodontoma, and indeed in one example there was no new calcified tissue deposited at all, even on the walls of the excavated cavity. This example was, however, a ground section, and since all the other specimens invariably showed deposits of primitive bone in the Howship's lacunæ of the dentine, serial sections might have discovered it here.

Nevertheless the use of the term "inostosis" is unfortunate, for not only is the primary feature one of tooth absorption but in no case was there continuity between the new calcified deposits on the dentine and the alveolar bone.

The lesion appears to be destructive so far as the tooth is concerned, but as the tooth disappears its place is taken by dense sclerosed and non-trabeculated masses of bony matrix. The case illustrated in fig. 4 (*g*) i and ii illustrates this. The root of the canine was so far eaten away by the growth that the tooth, which was to all outward appearance perfect, became intensely tender on pressure. The gums and the rest of the teeth were all strong and healthy. Histologically the pulp remnant was absolutely normal except for a trace of calcific degeneration and still showed a normal odontoblast layer. Osteoclasts were continuing to absorb the root in places, and elsewhere there was a deposit of calcified tissue on the absorbed surfaces. The two skiagrams were taken at an interval of two and a half years, and show the slow rate of progress of the lesion.

The structure of the sclerosed bone which had replaced the root is also particularly interesting. It is a solid non-trabeculated mass of bone matrix in which many of the bone corpuscles have died. There were a few vascular canals. It shows evidence of repeated alternations of absorption and deposition, so that it presents a mosaic appearance simulating Paget's bone. At one or two points near the edge of the sclerosed mass absorption and replacement were still going on and a few osteoclasts were found.

A specimen referred by Mr. Hubert Visick from one of his cases is also of great value because there are again two skiagrams but taken at an interval of only ten months. In the first there is little if any sign of the tumour, in the second it is clearly in evidence so that some examples of the lesion only require a few months to develop. In this specimen the new growth has invaded both the tooth and the bone of the septum to some slight extent (fig. 4 (*f*) i and ii). Furthermore, the neighbouring tooth has developed a granuloma at the apex in the interval, and though it is quite clear histologically that the infection has not spread across from one tooth to the other, it is nevertheless possible that some toxic irritation reached the cells and started the neoplastic change.

One of the most disappointing features of these tumours is that they are seldom discovered until the parodontal sulcus is invaded and sepsis has supervened. Nearly all the tumour cells have then been killed and replaced by leucocytes, so that the history of the lesion can only be read from its effect on the matrix (fig. 10). Fortunately, however, several of the cases, including that of Mr. Visick (figs. 9 and 4 (*f*) i and ii), do not fall into this category but show very clearly that the growth consists of undifferentiated cells which become either odontoclasts, osteoclasts or primitive osteoblasts quite indiscriminately.

Even when the cells have been destroyed the matrix provides evidence of dentine absorption, followed by deposition of primitive bone which has itself been repeatedly absorbed and replaced. Nothing could indicate more clearly the purposeless nature of this activity than the small islets of dentine which are left by the odontoclasts (fig. 10). It is not conceivable that the dentine in many of these teeth could have been contaminated in the first place or that there was any cause for inflammation, for the teeth were generally sound and healthy; but even if the dentine had been contaminated presumably these islets would have been contaminated too, yet they were spared and forthwith walled in with calcified matrix which itself, although it was freshly deposited tissue, was already falling a victim to the insatiable odontoclasts. This is particularly striking when compared with the progressive and purposeful way in which the derelict dentine is absorbed after infarction of the pulp (fig. 7).

Apart from incidental sepsis or loosening of the tooth, there appears to be no typical termination, and though there may be a general tendency towards bone deposition, tooth absorption continues; every case examined has shown the persistence of odontoclasts

unless they had been destroyed by sepsis, although some of the cases have had a known clinical history of more than three years.

Discussion

One view of the origin of an osteoclastoma would appear to be that, as it occurs only in cartilage bone and particularly in the region of the epiphysial cartilage, it represents a perversion of the preliminary destruction of calcified cartilage which accompanies the normal process of ossification (Geschickter and others, 1929). It is further suggested that the myeloid epulis is due to a rejuvenation of a persistent remnant of the absorption organ of the temporary tooth.

This view, of course, does not leave any vestigial remnant to account for the odontoclastoma. More important still, it does not take into account the evanescent nature of an osteoclast, the speed at which it works, or the probability that neither osteoclasts nor even osteoblasts, once they are differentiated, ever undergo mitosis and proliferate, for if they do not they cannot become neoplastic. Finally, no such hypothesis would account for the presence of the primitive calcified tissue of replacement in the odontoclastoma.

It appears that in both the odontoclastoma and in the endodontoma, as well as in the endosteoma, some hypothesis must be formulated which will account not only for the appearance of both the anaplastic osteoblast as well as the giant cell, but which will also account for their appearance in far greater numbers than could possibly be required for any purpose of repair.

It is first necessary to establish the fact of neoplasia; this thesis relies on the continual cell proliferation and on the absence of adequate known causation or typical termination in all these conditions, on the purposeless nature of the reaction, on the absence of law and order in the activities of the cells and in the absence of any inflammatory reaction or cellular infiltration of the tissues except where the growth has reached the surface and ulcerated. It is perhaps permissible to say that there is no other explanation which is in accordance with all the facts.

It is true that there are examples of chronic irritation of bone in which bone destruction and bone building are apparently indiscriminately mixed up. A good example is alveolar bone, which is constantly subjected to the ebb and flow of toxic matter absorbed from an ulcerated gum margin, but the condition is not active like these lesions described above. In pyorrhœa there are old Howship's lacunæ, and these have often been filled up again with more recent bone-deposits until the matrix may present the mosaic appearance of Paget's disease, but it is rare to see an osteoblast in an active phase or even to see an osteoclast at all.

Quite the nearest approach to the histological picture of these bone lesions is that of generalized osteitis fibrosa, where the parathormone appears to stimulate all types of bone cell to increased activity. At first it stimulates the production of osteoclasts, then, in experimental animals, as the organism gets used to the hormone, there is a reversal in its action and osteoblasts predominate (Selye, 1932*a* and *b*). It is not, however, possible to imagine the *localized* production of such a growth stimulant in these lesions; or alternatively, if it were, the postulated substance would be little short of the missing ætiological factor in neoplasia itself.

One difficulty in adopting the diagnosis of neoplasia in the endosteoma and endodontoma is the presence of several different types of cell all increasing in number as the lesion grows. It could, of course, be argued that if the osteoblast were the true neoplastic cell then the matrix it produced in the middle of the bone or in the pulp would set up irritation and thereby cause the production of osteoclasts, but there appear to be too many osteoclasts for this explanation, and, furthermore, the osteoclasts seem to start the lesion or at least gratuitously to extend it by boring out the dentine or existing bone (fig. 6 (*d*)).

It is not, however, necessary to consider this theory or even, in this connexion, to consider whether osteoblasts can proliferate; for since a similar lesion has appeared in the dental pulp where there are not normally any osteoblasts there must be some other explanation of their origin.

It is however known that both osteoclasts and a primitive type of osteoblast as well as fibroblasts can appear in the pulp in response to irritation, though they are not normally present, and it can only be supposed that they are evolved from the undifferentiated mesenchyme cells which form a part of the normal cell content of the pulp. It is equally only possible to suppose that these primitive cells are responsible for the endodontoma, and, by analogy, for the endosteoma since these same cells are present in bone.

It is at least reasonably definite that a lesion consisting of undifferentiated connective tissue cells, together with many osteoblasts and osteoclasts, has appeared in the tooth pulp, and it has been established (cf. Fish, 1939*a* and *b*) that the latter types develop by differentiation from the former. If then the corollary is true and fully differentiated osteoblasts and osteoclasts do not themselves proliferate, an interesting theory of "heterogeniture", that is, the production by mitosis of two cells having different potentialities, emerges to account for benign neoplasia in bone; for it must be supposed that only the undifferentiated cells are the truly neoplastic elements. The daughter cells, produced when they divide, may either differentiate into osteoblasts or osteoclasts and cease to be neoplastic or alternatively they may remain neoplastic and continue to divide, but in that case they will fail to differentiate. Naturally some of their offspring must do one thing and some the other since osteoblasts continue to appear and neoplastic proliferation also continues. Whether the choice depends on some inherent property in the cell or upon its environment is not clear.

Such a theory would explain several features of neoplasia in the calcified connective tissue; for example, the numerous and ill-defined gradations which are observed between the pure osteoclastoma on the one part and the purely proliferative ivory exostosis at the other extreme. Then again, the smaller the proportion of new cells which differentiated the less would be the bone matrix either built or absorbed, but the more malignant would be the growth, and it is observed that the most malignant bone tumours do not in fact produce many osteoclasts or a relatively high proportion of fully differentiated osteoblasts or much bone matrix.

There is also a well-graded series in this respect, showing a progressive increase in the proportion of embryonic cells and a reduction in the number of the differentiated adult variety. The series includes the ivory exostosis, the bony epulis, the endosteoma and endodontoma, the less well-defined, but still focal, osteitis fibrosa and possibly leontiasis ossea, if these be indeed neoplastic; then follow osteogenic sarcoma in several varieties until at the end of the series a round-celled sarcoma of bone showing practically no tendency to differentiation or, of course, to matrix formation is observed. The relative absence of mitotic figures in the benign endodontoma, endosteoma and odontoclastoma suggests that most of the undifferentiated cells are resting or perhaps destined for differentiation.

Finally the non-malignant though locally destructive character of the osteoclastoma is explained for the osteoclast appears as a fully differentiated cell, not as a proliferative embryonic type. It will not therefore disseminate, although its predatory nature makes it locally destructive.

To take the corresponding example in the closely related soft connective tissue, a simple fibroma is differentiated from a spindle-celled sarcoma, and that in turn from a round-celled sarcoma by the proportion of new cells which differentiate and deposit collagen fibres compared with those which remain anaplastic and proliferate but produce no fibres.

The factor which determines in bone neoplasia whether the new cell shall be an osteoblast or an osteoclast is obscure. In mechanical, chemical or bacterial irritation it is the intensity of the irritant which determines the result and not, apparently, any factor inherent in the cell. This is seen from the fact that the type of cell produced at any given point when thymol is introduced into bone (fig. 1) depends on the proximity of the irritant.

Whatever may be the nature of the "urge" in neoplasia it seems to vary from time to time in bone tumours, for actively destructive lesions will gradually become almost purely proliferative, until the new matrix practically extinguishes the cellular elements and clinically the growth appears to have undergone a spontaneous cure, or "calcification" as it is wrongly called, which throws a doubt on its neoplastic nature. It is extremely doubt-

ful, however, whether it is ever really cured. There were still a few embryonic cells and some osteoclasts high up in the densely sclerotic bone which had replaced the root in fig. 4 (*g*), though this area had been sclerotic for at least two and a half years. Moreover, the dense new matrix is a mosaic and not by any means normal bone, and indeed many of its cells were dead.

The bone and tooth tumours are not the only neoplastic lesions which require some theory of heterogeniture to explain them. All tumours, in which highly specialized cells appear, present the same problem. It is not, for example, to be supposed that a multipolar nerve cell in a ganglio-neuroma is the actual progenitor of other multi-polar cells; yet this cell is present in great numbers and its orgin has to be accounted for. Nevertheless it is not itself likely to be the actual *neoplastic* cell.

It is reasonable to inquire in this connexion why none of the cells in the endodontoma have differentiated into odontoblasts. The reason may perhaps be that the cells of the dental papilla in the embryo do not differentiate into odontoblasts except in the presence of the dental epithelium (Glasstone, S., 1939), and this element is, of course, lacking in the adult pulp.

In conclusion it may perhaps be felt that these tooth tumours, if indeed they are tumours, have little clinical significance, but it may not be too much to hope that their investigation may help to shed light on the nature of benign neoplasia in bone or even on the wider issues. It would at least appear to be desirable that in recording future cases the conditions described as endodontomata and odontoclastomata respectively should not be confused or grouped with the results of inflammation or infarction of the pulp. It is particularly desirable also that cases such as that shown in fig. 5 be looked for in which there is no abnormal communication with the periodontal membrane. The closed crucible of the tooth pulp excludes many of the distracting features of the corresponding bone lesions.

The author wishes to express his indebtedness to Mr. Handfield-Jones, Mr. Rae Shepherd, Mr. Everard Turner, Mr. Hubert Visick for contributing specimens, to Dr. Courtney Gage (fig. 2) and Dr. Shires (fig. 4 *g* (i)) for the loan of skiagrams, to Mrs. Lindsay for the references, and to Mr. William Pereira for cutting all sections and making the photomicrographs and tracings, and to the Medical Research Council for a grant towards the expenses of the work.

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Professor W. E. HERBERT said that he was particularly interested in those cases of absorption of the dentine from the pulp side which Dr. Fish had shown as being the result of trauma.

He had kept records of a good many cases of complete calcification of the pulp following trauma and was of the opinion that this commonly occurred when an anterior tooth in a young patient received an injury insufficient to cause gangrene of the pulp. He imagined that absorption of the dentine from a similar cause was far less common.

He had records, however, of one case where the two conditions had occurred in adjoining pulps as a result of the same injury.

Case in which calcification of the pulp, and absorption of the dentine from the pulp side, had occurred in adjoining teeth following the same injury.

The patient, a girl aged 19, had attended the Dental Department at Guy's Hospital in October 1937, and in the course of a routine examination the upper right central incisor was found to be discoloured. There was a history of a hockey injury five years previously. On examination the upper right central incisor gave a slight but definite response to thermal changes whilst the upper left central gave none. Radiographs showed the pulp chamber of the upper left central to be completely calcified whilst that of the upper right central was larger than normal, suggesting the condition of pink spot.

Section of Surgery

Chairman—J. B. HUNTER, M.C., M.Ch.

[*March* 5, 1941]

DISCUSSION ON WAR INJURIES OF THE SPINE

Mr. Julian Taylor: In his Goulstonian lectures of December 1915, based on his collected records of 300 patients, Dr. Gordon Holmes told us nearly everything we know of war wounds of the spinal cord. Ten years later the Medical Research Council published an excellent monograph on the same subject.

My own first experience of war wounds of the cord was in the early months of the last war when one of my stretcher bearers aged as it proved 16, fell suddenly paralysed in Polygon Wood, having been hit by a machine-gun bullet in the back. There was neither shock nor pain, but there was a puncture and a complete paraplegia from the mid-thoracic region downwards, which apart from the neurological evolution of transection of the cord, persisted unchanged until he died soon after the Armistice, not yet 21. The story is characteristic of spinal wounds now as then, for there is still that gloomy contrast between the unchanged prognosis for injured cord and the remarkable improvement in cases of treatment of the fractured column. The reason for this contrast is readily seen: whereas with injured bones, and indeed with injuries of most soft parts, once some sort of mechanical repair has been effected, the body takes care of the return of function, in the central nervous system the surgeon may contemplate no such reward for his services. For here once an axon be divided or a nerve cell killed the resulting demyelination is permanent. When also we remember how narrow a bottle neck is the cord in the pathways from the relatively enormous brain to the vast periphery, we have the explanation of two salient facts: first that injuries of the cord most commonly cause permanent paralysis, second that a small volume of trauma has disastrously extensive consequences. In both these respects injury to the cord is a far greater catastrophe than is injury to the brain.

War injuries fall into two classes, the larger which we may call the *civil group*, characteristic of our civilized age and at present usually caused by motor-cars or falling masonry, the smaller comprising those that may be included in the *projectile group*; the damage to the cord and to the bodily functions is similar in both. The importance of the cord to the body and also its extreme fragility are indicated by the perfection of its protective apparatus, of which the vertebral column is almost incredibly strong yet beautifully mobile, the contents of the spinal canal a marvel of hydrodynamic perfection. When we deprive the cord of its fluid bed at operations we know that no more than a rough touch on its bare surface may cause irreparable damage, and it is therefore not surprising that a force great enough to penetrate its natural protections, on reaching the spinal cord crushes it in general severely. There is thus in all cord injuries and in both groups a high proportion of neurologically complete interruptions.

Varieties of Interruption of Conductivity

Interruption of conductivity of the cord may be due to one or more factors. Thus there may be complete severance, there may be physiological interruption due to crushing without section, or there may be what is called spinal concussion or spinal shock. These are instantaneous, but in addition there is usually some bleeding later at the site of crushing, and this bleeding tends to spread up and down the substance of the cord in more

or less cylindrical form, giving place still later to cavities containing clear fluid. In a complete lesion the downward spread does not cause much that is recognizable in the clinical picture, but the upward is one of the many things that in cord symptomatology causes alteration of skin sensibility above the neurological levels of cord lesions. The effects of all these agencies, save severance, on the conductivity of the cord, may be transient, and thus it is clear that part of the immediate effects may be due to temporary causes, and part to permanent. Theoretically by adding a fraction of temporary to a fraction of permanent we may make a complete interruption, and thus we should not be able to say what is the chance that an immediately complete paraplegia may improve and to what extent. But in practice this does not hold good, for it was the experience of Sargent and of Trotter that with early complete paraplegia, no return of function is seen. The contrary has been stated so often that I have looked for first or second hand evidence of recovery in such cases, but I have never met it. There must be some explanation of such an important divergence of opinion, and I believe it is found in the following possibilities: (1) That a sufficiently accurate investigation of skin sensibility may not always be carried out, early complete paralysis being a well-known occurrence in partial lesions where sensibility is preserved though impaired. (2) In the observation of what is called spinal concussion. Spinal concussion may be regarded as a suspension of the functions of the cord which clears up within some hours or a few days after an accident, and is thus unassociated with severe or continued crushing of its substance. It is possible that if one were able to examine a number of cases just after accidents, one might find some where concussion had caused complete paraplegia and impenetrable anæsthesia, but if so the beginning of recovery would not be long delayed. In fact by the time that one usually sees these cases after accidents the concussion element, even if it has been severe, is passing off and the lesions are thus obviously partial in nature. In my opinion complete paraplegia and severe concussion are thus easy to distinguish as the hours pass and thus we may perhaps modify Sargent's rule into the view that a paraplegia still complete after a day or two does not recover. The acceptance of this piece of clinical experience must determine the aims of treatment for if function cannot return, what reason is there for attempting to free the spinal cord from pressure?

The facts regarding the injured *cauda equina* are a little different, for its filaments have not quite the fragility of the cord and may be compressed without utter destruction. However the hold on life that these structures are apt to display may have unpleasant consequences in the form of persistent pain in their distribution.

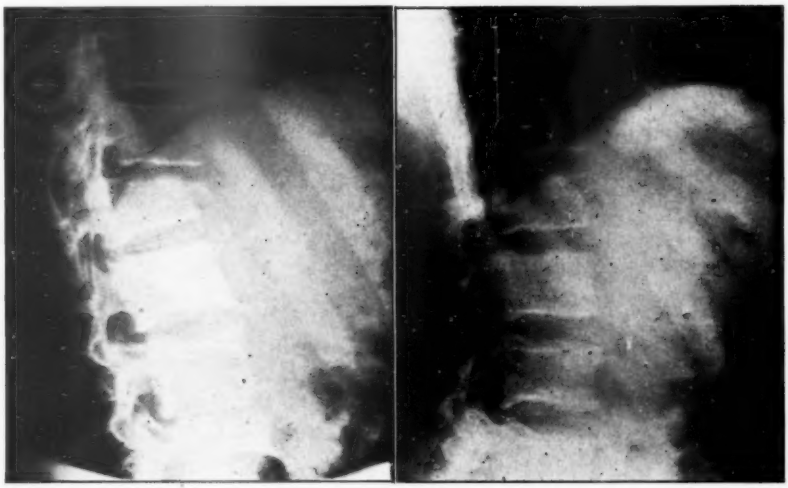
The partial interruptions.—As opposed to spinal concussion, hæmorrhage into the substance of the cord, being progressive, is capable of producing increasing degrees of interruption after an accident, the increase at first being due to actual continued effusion of blood, and later to the reaction to its presence in the tissues of the cord in the neighbourhood.

Clinically the existence of a partial lesion may be recognized early by persistence of either skin sensibility, motor power, or reflex activity below its site. I need no more than mention the normal occurrence of spasticity with increased jerks and extensor responses later in the story of the complete lesion. And before leaving the clinical examination of such cases I should say that there is what may be called the academically incomplete lesion, one that shows during its later history that it was not quite complete, but which, though some slight return, say, of sensibility may be seen, gives back no useful function.

Return of function in partial interruptions.—Though in my experience partial lesions show early or at once their nature, they do not proceed to complete recovery either invariably or rapidly. As has been indicated the occurrence of bleeding into the cord substance may increase the extent of the clinical picture during the first fortnight, and when hæmorrhages become encysted they may be found in conjunction with permanent defects of conductivity. However, the fact that a lesion is a partial one, indicates that the violence that reached the cord was slight, and thus we may justifiably hope that useful recovery may occur, though the duration of the recovery period may last as long as a year. In the *projectile group*, wounds causing partial interruption seem to recover to a lesser degree than do those of the *civil group*. This was Holmes' opinion in 1915 and it is confirmed in the M.R.C. Monograph, where it is stated that from the whole war only 36 partial interruptions had been followed to results, and that all had serious disabilities.

Treatment.—The only cases that from the cord point of view are worth operative or manipulative treatment with the object of relieving pressure, are the partial lesions the recognition of which has been discussed. Experience of the present war has suggested that partial lesions are of considerable rarity in both groups. In 300 cases Holmes found 45 incomplete lesions, the cauda equina not included. Therefore in less than a sixth of the projectile cases we may consider the question of surgical relief of pressure, and even in the majority of these we shall reject it.

The relief that may be given to the cord in certain incomplete interruptions.—*Civil group*: In the local relief of cord pressure in the civil group where manipulative reduction proves impossible, operative reposition is often easy. It is hard to admit when case after case presents itself with complete paraplegia that all we can do for these often young men is to nurse them. Recently we had a dislocation unrelieved by manipulation, which was reduced by operation. Fig. 1 (*a* and *b*) shows skiagrams of this before and after reduction with perfect result. However, the patient is as completely paralysed after as before the operation.



(*a*) (*b*)

FIG. 1.

Projectile group: Here we have to decide in which cases early or late explorations are advisable for the removal of metallic or bony fragments. If there be an early complete lesion there is no neurological reason for doing so. But if the lesion is incomplete then there *may* be persistent pressure on the cord and it *may* be worth relieving. It is rare for metallic fragments to be held up in the spinal canal, a projectile having the energy necessary to penetrate the canal or fracture its walls, having usually enough left to carry it out again into other tissues, such as the soft parts or sometimes the substance of the vertebral bodies. I think my colleague Mr. Harvey Jackson had an example of a very large shell fragment lodged in the canal, but the smaller ones rarely stay inside it. Figs. 2 and 3 (*a* and *b*) show bomb fragments in the tissues outside the column, associated with interruption of the cord and cauda equina, respectively; fig. 3 being from one of Mr. Jackson's cases. In a partial lesion as may occasionally be found accompanied by a fragment stuck in an intervertebral foramen, or by a fragment of metal or bone inside the canal and therefore possibly making continued pressure on the cord, the exact situation of the fragments may be recognized precisely by stereoscopic skiagrams. Such an event as the association of a partial lesion with a fragment so placed

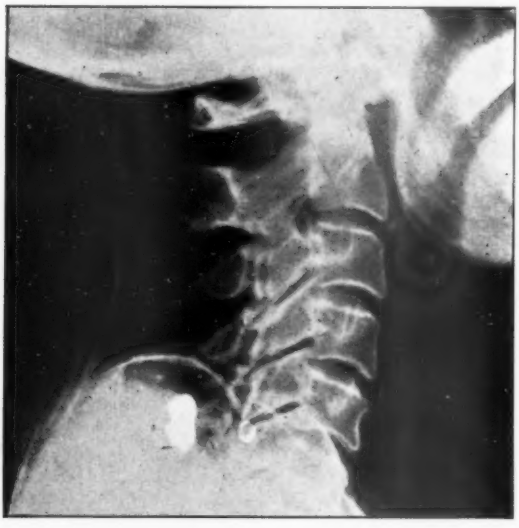
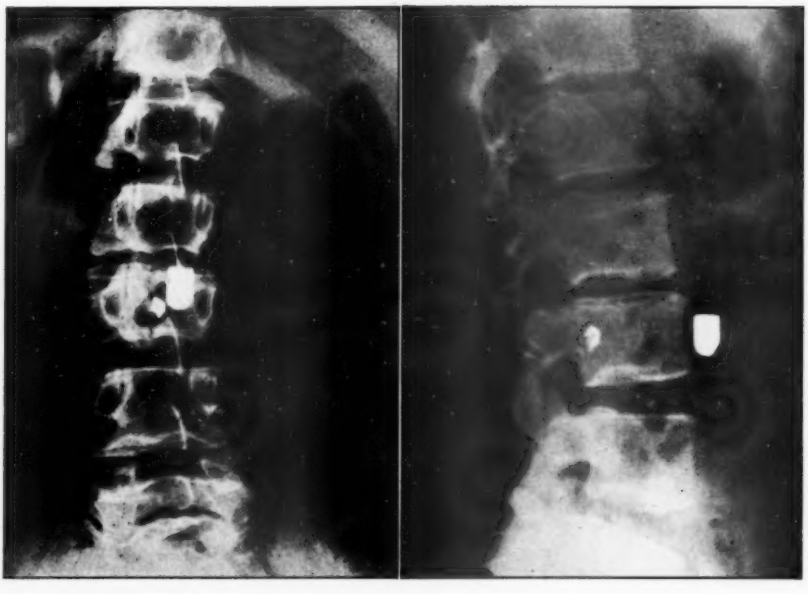


FIG. 2.



(*a*) (*b*)

FIG. 3.

is so rare that I have not yet attempted to remove a single metallic fragment from the spinal canal during this war, and did so only once during the last war, and then probably unnecessarily.

Infected Wounds and Meningitis

The other reason for removing metallic fragments is the prevention of infection irrespective of the position of the metal. Bearing in mind that an infected track must pass by the cord or meninges, an infected wound is an obvious source of meningitis. Meningitis may be subsequent on the wound alone or it may follow attempted or successful removal of metal, clothing or bone. It is obvious that where, as has usually been the case in our patients, entrance wounds are suppurating freely already, the danger of operations is greatly intensified especially where the foreign body is close to the meninges. These wounds should be brought to as clean a state as possible by a superficial drainage operation before removal of the metal. Cerebrospinal fluid fistula in such cases is a formidable complication and one which calls for delay until wounds are really clean before undertaking any operation, other than drainage. Many such fistulæ heal spontaneously. Meningitis in penetrating wounds of the central nervous system is extremely common in neglected cases, but the mortality from it is low, as the meninges seem to be capable of dealing with their infections. The infected focus should be cleansed efficiently and with as little disturbance of the membranes as possible. In addition we have the new bactericidal drugs; but these are to be considered rather as adjuvants to surgical treatment; M & B 693 has in certain cases cleared up even staphylococcal meningitis when no other treatment, not even by lumbar puncture, has been employed.

No operation should be undertaken in a penetrating wound of any part of the central nervous system unless stereoscopic skiagrams be available; urgency of operation is not so great as in head wounds because the danger of meningitis is less in spinal cases; and as nearly all these unlucky people have complete interruptions, the presence of suppurating wounds does not add very greatly to their already sad state.

In five cases out of six transport, nursing, and the management of the bladder form the entire treatment.

Transport.—As practically all the projectile cases have complete lesions, the position in which the patient lies is of great importance neurologically.

Nursing.—Experience in this war has shown us that the primary needs with the anæsthetic back are distributed pressure, continual changing of the sites of pressure over bony prominences, and cleanliness of the skin. Whereas water beds and sorbo rubber mattresses permit all of these, a plaster bed does not encourage the last two which are certainly as important as any. Our experience of patients sent to us with anæsthetic backs on plaster beds has been that there has been a bedsore of formidable extent and of a depth to be guessed only by the pessimist. We find also that using water beds we are able to reduce quickly the amount of hypnotic given so that it may be presumed that the fractured column is not disturbed unduly. In cases of the civil group with complete or nearly complete lesions our experience is that if cutaneous anæsthesia extends up to the buttocks or above the first lumbar peripheral nerve segment or higher, plaster cases are unjustified by results. There can be no neurological improvement in prospect and the backs are just skinned. A water bed or even half a water bed is the best thing for them. In the incomplete case where a lesion is capable of functionally useful recovery, there appears at a quite early stage enough cutaneous sensibility to prevent the occurrence of serious pressure sores.

The bladder.—Retention of urine occurs in nearly every case of cord or cauda equina injury. It is the predisposing cause of the urinary infections that eventually destroy most of the victims of cord injury. Its management is the primary duty of the medical attendant.

It is most important to recognize that retention of urine is present as it almost invariably is. There may be little urine secreted early owing to general shock, and when secretion does begin, the patient may be insensible of his full bladder. To leave the patient until his bladder makes a visible bulge in the abdomen, and then to pass a catheter without extreme cleanliness, is running a risk of disaster.

Management of the bladder may be by:
(1) Regular catheterization.
(2) The use of the tied-in catheter.
(3) Suprapubic drainage.

FIG. 4.

(*a*)

(*b*)

FIG. 5.

All are capable of producing serious urinary infections and each has its disadvantages. Whatever method be selected, it must be carried out with the utmost care.

(1) *Regular catheterization* must be carried out eight-hourly, and this is especially important when the patient, improving in health, is eating and drinking normally. The disadvantage is that the bladder may fill unduly during the intervals unfelt, and may thus open the pathway for infection of the kidneys. It is, however, the only way of preventing infection of the urinary tract.

(2) *The tied-in catheter* entirely prevents distension of the bladder but is often the cause of serious urinary infection. Fig. 4 is a skiagram of the bladder of a patient with an old cauda equina injury, after having had a catheter tied in for many months. There were several stones in the bladder and prostatic urethra, the left kidney had already been removed leaving a sinus in the loin, and there was recurring renal colic with high fever. Fig. 5 (*a* and *b*) shows in the intravenous pyelogram the contracted bladder and the distended right kidney.

The reason for the liability to infection inherent in this method is the fact that with whatever care, and frequency, a catheter be changed, it is impossible to avoid the occurrence of urethritis. It is true that the employment of one of the antiseptic-sealed pressure-regulating apparatus such as the Dukes' or the Monro's minimizes the severity of the resulting cystitis. The supervision of these machines needs constant care by doctors and nurses and if, for example, a new night nurse does not understand them she can spoil everything. I have known in my own practice two deaths following the introduction of these methods in my absence. Regular catheterization by a resident officer is, however, independent of the constant changing of nurses. The disadvantage of intermittent emptying is that the bladder is not kept undistended perforce, but in my experience no harm results if one does not grossly infect the urine and one empties the bladder completely. It is not necessary to infect the urine provided the resident officer carries out the work himself and knows what he is at, and provided also that an adequate supply of catheters in good condition is always available. One may even clear up cystitis by this method when the urine is already grossly infected, and I will cite the case of a paraplegic admitted to hospital with a tied-in catheter and a stinking ammoniacal urine thick with pus. He was catheterized regularly by my assistant, and three weeks later the report on the urine was: "The deposit shows epithelial debris and a few pus cells. Culture *Staphylococcus albus.*"

It is when we are expecting a return of function to the bladder that the system of regular catheterization is far superior to any other, for a clean urinary tract and an unspoiled urethra are the best inducement to the central nervous system to re-establish micturition. To quote another example, a doctor suffering from a spinal tumour had his bladder emptied some ninety times by three young men before micturition came back. There was never more than an occasional pus cell in the urine which was examined regularly throughout the period of retention.

(3) *Suprapubic drainage.*—This method always results in cystitis though the bladder is always empty. It is unsuitable where micturition is likely to return, as such fistulæ may be slow to close and may be a discouragement to progress. It is also held by some to result in leaky wounds where abdominal walls are paralysed. I have not found this with the use of the small transverse incision which makes a good watertight joint.

I therefore recommend:

For the patient who may recover his vesical function—Regular catheterization.

For the patient likely to develop automatic micturition—Regular catheterization.

Automatic micturition is not entirely satisfactory but in the male subject it is not a bad compromise. It is our custom with such patients to continue to empty the bladder once daily by catheter if possible just after automatic micturition. The results are good and cystitis is slight.

For the patient who is not going to improve and who is not going to develop automatic micturition, for example in a cauda equina lesion, suprapubic cystostomy with lavage of the bladder at low pressure is best.

For the patient who has to travel in an ambulance a long distance, and in the field in this war of mobility, a catheter tied in and scrupulously arranged is probably the least harmful system.

Mr. R. Watson-Jones: In days of peace, the most frequent injury of the spine is a simple compression fracture of one or more vertebral bodies, uncomplicated by crushing injury of the spinal cord. The civilian surgeon is called upon to treat twenty or more uncomplicated fractures, for every fracture with paraplegia. In days of war we are inclined to believe that spinal cord injuries must loom more prominently. The title of this discussion, "War injuries of the Spine", suggests the clinical picture of a bullet embedded in the spinal canal, or of a spinal cord transected by fragments of shell casing. These nerve injuries are of great importance to the Army Medical Service, but my investigations show that surgeons of the Royal Air Force, of the Royal Navy, and of the Emergency Medical Service, are faced to-day, exactly as in days of peace, with a large number of uncomplicated fractures, and a small number of spinal cord injuries.

Avulsion Fracture of Spinous Processes

Even the avulsion fracture of the 7th cervical or 1st dorsal spinous process, known as "shoveller's fracture", may be described as a war injury. One spinous process is torn from the vertebra by violent contracture of the rhomboid muscles at the moment that a labourer drives his shovel into wet clay, or at the moment that he flings his heavily laden shovel in the air. Until recent months this injury was almost unknown in this country. It has now become relatively common. This recent frequency is no doubt due to the strenuous digging of war time, which continues in wet weather as well as fine, digging trenches across golf links, excavating underground shelters, and clearing the weighty debris of demolished buildings. But although British surgeons have only now begun to recognize the shoveller's fracture, Matthes treated 107 cases in two years, and Debuch reported no less than 187 cases in sixteen months. There may be many reasons for the report of such amazing series of injuries in 1937 by two Continental surgeons, but the fact that Germany's war preparation was already fully developed by that date is of significance.

The Mechanism of Spinal Injury

Compression or wedge fractures of vertebral bodies in civil life are usually due to falls from a height in the standing or sitting position. A dock labourer falls from a deck into the ship's hold; a window cleaner falls from his ladder; a steel erector falls from scaffolding; a suicidal maniac jumps from an upper window; from all these accidents crushing fractures of the vertebral bodies are sustained at the dorso-lumbar junction. If the patient has fallen in the sitting position the spinal injury may be the only fracture, but if he falls in the standing position, the os calcis of one or both feet is also crushed.

Less frequently, fracture of the spine is due to forcible flexion of the trunk. A miner in a pit is crushed by a fall of roof, and the weight of rock and debris, crashing on to his shoulders doubles up the spine like a clasp knife. Forcible flexion movement drives the anterior angle of one vertebral body into the middle of the vertebral body below, comminuting the bone, displacing marginal fragments forwards and rupturing the intervening fibro-cartilaginous disc.

Spinal Injuries in the Royal Air Force

The same two types of fracture may be recognized in the injuries of the spine which are sustained by members of the Royal Air Force. A pilot baling out from an aircraft at night, may strike the ground sooner than he expects, and fail to make allowance, by flexing his knees and hips, for the ten or fifteen foot drop to which a parachute landing corresponds. If his parachute has been damaged the violence of impact may be even greater. For instance one pilot in baling out at 20,000 feet struck the tail of his aircraft and was rendered unconscious. He regained consciousness before landing, to find the parachute harness twisted round one knee by which he was suspended, both shoulder-joints dislocated, and four panels of the parachute torn. His landing was unduly heavy, and to the injuries already sustained were added the further injuries of a crush fracture

of the os calcis and a crush fracture of the spine. It is typical of the courage and endurance of these men, that despite cerebral contusion and concussion, dislocation of both shoulder-joints, rupture of the knee-joint ligaments, a comminuted fracture of the os calcis necessitating subastragaloid arthrodesis, and a crush fracture of the spine, this boy of 19 was flying once more within seven months of his injuries.

Other members of the Royal Air Force sustain vertical compression of the spine in less dramatic manner. One was on guard on the roof of a building, and owing to the black-out, stepped off into space, crashed sixty feet to the ground and fractured his spine. He picked himself up, walked to the Station Medical Officer and reported sick! Another was walking across an aerodrome in broad daylight, slipped in the mud, and sat down heavily. He had not only fractured his spine, but had also sustained fractures of the scaphoid bones of both wrists and of the head of the radius of one elbow!

The second type of fracture, where the spine is forcibly flexed, may be sustained by pilots and air crews on crash landing. The pilot is sitting in the cockpit with his feet on the rudder bar, and his lower limbs and pelvis relatively fixed. The upper trunk swings forwards with momentum and violent flexion occurs at the dorso-lumbar junction causing fracture of the spine. This injury is actually much less common than would be expected, and it has been found that if a fracture is sustained at all, it is in the upper dorsal or lower cervical spine. The reason for this unusual localization lies in the special harness which is generally worn by pilots. The harness which permits aerobatics, holds the pilot in his seat and passes over the front of both shoulder-joints. It limits the forward fling of the trunk which would otherwise occur, minimizes the violence of injury, and raises the site of angulation from the lumbo-dorsal junction to the upper dorsal level.

Fractures at this level are very difficult to reduce. The success of postural reduction of fractures of the dorso-lumbar junction of the spine by simple hyperextension between two tables, lies in the tremendous power of leverage of segments of the spine above and below the fulcrum. But if by protective harness the fracture is localized to the upper dorsal level, it lies in the middle of one of the arms of leverage and not at the junction of the two. But for the very reason that reduction is difficult, perfect reduction is unimportant. Since the injury is in a relatively immobile segment of the spine, malunion is not penalized by persistent pain. It has been found possible to reduce the period of immobilization, and provided that perfect tone has been maintained in the spinal musculature, by exercises performed for five minutes every hour of the day throughout the period of immobilization, officers in whom the duration of incapacity is of vital importance, have been returned to full flying duty in less than half of the usual incapacity period of nine to twelve months.

Spinal Injuries in the Royal Navy

In the Royal Navy the spine is usually fractured by vertical compression. A member of the Merchant Service fell from the crow's nest down the inside of the mast. The confined space kept him upright, and the impact caused fractures of the os calcis of both feet, and of one lumbar vertebra. When a torpedoed ship is heeling over and sinking, the sailor usually scrambles to the uppermost side of the deck before jumping. But if he is to clear the bilge keel which now appears above the sea level, the jump must be much wider than it would appear, and unless the man is experienced in the art of leaving sinking ships he may well land, not in the sea, but on the bilge keel or ship's side, and crush both his os calcis and his spine.

More frequently the sailor sustains this dual injury without ever leaving the deck. The fractures result from the explosion of a mine below the vessel. Instead of the victim crashing down from a height and striking the deck, the deck comes up and strikes the victim. The effect is the same. In a recent explosion at sea, nine sailors in one ship were injured in this way. These men must often struggle in the sea, maybe for considerable periods, despite their fractures of feet and spine. On other occasions the sailor is lying flat on his back, on the deck, or in his bunk, and the explosion beneath the ship flattens his lumbar lordosis with such violence, that one or more vertebræ in the middle of the lumbar curve are crushed. I have heard of one rating who was lying in this way when a mine exploded beneath the ship. After an appreciable interval he sat up to collect his wits, and then for the first time, suddenly felt power and sensation

disappear from his waist downwards. Presumably the explosion fractured his vertebra and ruptured the posterior ligaments, and when he sat up and carried body-weight through the injured region, the upper segment slid forwards and damaged the cord.

It is unnecessary to discuss at length the treatment of lumbo-dorsal fractures, but I would emphasize the four most important points: (1) The compression can be completely reduced by hyperextension of the spine, by the two-table method, but the limit of hyperextension must be reached. The tables must be so far apart that the pelvis tilts forwards. Hyperextension of the lumbar region must be complete. If the lower table is too close to the upper, and supports not only the thighs but also the pelvis, hyperextension is incomplete and reduction of the fracture is imperfect. (2) The fully hyperextended position must be maintained by an adequate plaster jacket which extends from the clavicles to the symphysis pubis. Short jackets, and jackets in which a large abdominal window has been cut before the plaster is thoroughly set, so that the plaster cracks at this level, are often responsible for imperfect results. (3) In lumbar fractures, the fully hyperextended position must be maintained for not less than four months. Immobilization for too short a period allows the comminuted vertebral body to crush once more. Late compression cannot be prevented by a posterior spinal support. As a general rule supports of this type are not only useless but actually harmful, because they aggravate the psychological disturbance which may arise when a man "breaks his back". (4) From the first day after reduction of the fracture, and throughout the period of immobilization, the patient must practise hyperextension exercises and maintain the tone of spinal musculature. A man who fractures his spine should come out of plaster after four months, with better muscles and a better poise, than he had on the day of injury.

When the spinal cord or cauda equina are crushed, the best method of relieving nerve compression is not by laminectomy but by reduction of the bone displacement. In the lumbar region where the medullated fibres of the cauda equina are injured the prognosis is relatively good. In the dorsal region recovery from complete paraplegia is exceptional. If sensory loss is quite complete and persists for more than ten or fourteen days, it is almost certain that the cord has been transected and continued immobility in plaster is of no value. In all other cases, reduction must be maintained by a plaster jacket, or plaster bed and turning case. The fear of trophic sores, and the difficulty of management of the paralysed bladder, should not prevent a surgeon from continuing immobilization in plaster. I do not suggest that in these circumstances no trophic sores will develop; but trophic sores are no more liable to occur beneath plaster than if a patient is treated on a water bed. No treatment can always prevent ulceration of the skin, but if the plaster is carefully moulded so that it fits every contour, and is changed whenever the patient alters in shape owing to gain of weight or loss of weight, the pressure is so evenly distributed that trophic ulceration is minimized. Moreover, we know that this type of ulceration of the skin is best treated by the "vaseline gauze no dressings technique", and even if sores do develop, plaster immobilization should continue.

Spinal Injuries in Air-raid Casualties

Fracture of the spine is unusual in air-raid casualties. A few patients are buried in debris, and sustain forcible flexion of the spine with comminuted fractures of the second type. But as a rule, falls of masonry which are sufficient to fracture the spine, are also sufficient to kill the victim. A certain number of dislocations and fractures of the cervical spine have occurred in demolished air-raid shelters where the heavy roof of the shelter has fallen on the heads and shoulders of those within. In the treatment of cervical dislocations the value of skull traction calls for emphasis. Skeletal traction from the skull is the safest method of reducing a fracture dislocation with over-riding of the articular processes. Moreover, it is the best method of preventing redisplacement. Cervical dislocations are liable to redisplacement even despite complete immobilization in plaster, especially if the upper margin of one of the articular processes has been fractured. With continued traction for three or four weeks by means of skull callipers and a weight over the head of the bed, redisplacement can be prevented. Finally, skull traction is the safest method of relieving pressure on the cervical cord, because it not only reduces bone displacement, but by maintaining a distracting force on the intervertebral spaces, it promotes replacement of retropulsed intervertebral disc material.

Mr. K. I. Nissen : The country branch of our orthopædic hospital is one of the special centres for the treatment of spinal injuries.

For the prevention and treatment of pressure sores in paraplegic patients, nothing can equal a skilfully made plaster bed. No time must be lost and I aim at having the bed mounted, lined, and the patient in it within twenty-four hours of arrival. The usual plaster bed, which ends just above the knees, has been found insufficient for several reasons. Œdema occurs where the plaster ends, and if the heels are protected in below-knee casts, the œdema may determine transverse linear ulceration above and below the back of the knee. There is always a tendency for the flaccid lower limbs to be rotated and pressed inwards during bedmaking, and so to develop sores over the medial femoral condyles.

The full-length plaster bed has proved excellent in practice. It takes some skill to make one which is wholly satisfactory, and a few special points may be of interest. The patient lies face downwards with hips and knees slightly flexed, the legs including an angle of 20° to 30° and the feet at right angles. A thin layer of gauze covers any sores. A layer of padding half an inch thick is strapped or bandaged over the trochanters, and round the knees and ankles. The bed is then made of twelve double thickness layers of gauze soaked in plaster cream, and extends from the nape of the neck to beyond the toes. The nursing area is no wider than three inches, and ends at the top of the natal cleft in a sharply pointed arch. A common error is to make this area too wide and like a Norman arch. Severe gravitational œdema and prolapse of the buttocks then result in bilateral linear ulceration at the edge of the plaster. The bed is mounted on blocks high enough to allow the easy insertion of a bedpan. The bed must be level in both directions. If tilted to one side œdema of the lower buttock results ; if tilted downwards, sores on the soles of the feet. The edges of the nursing area and the plaster in relation to any sores are very easily protected from soiling by applying gauze squares which have been soaked in liquid vaseline. The lining of the bed consists of home-made Gamgee tissue enclosing a half thickness of the standard white wool.

Any deep sores are filled with layers of dry gauze up to the level of the skin. This ensures even pressure. The patient is turned out of his bed as infrequently as the discharge of the sores permits. It is most gratifying to see sloughs down to bone finally give place to level supple skin.

Paralysed patients soon become stiff. All limbs, paralysed or not, need to be put through the fullest possible movements every day. The hips and knees in particular must be able to reach at least 90° to allow irrecoverable cases the early opportunity of an armchair.

A number of less severe fractures have been admitted in plaster jackets. For various reasons three out of four have had to be reapplied sooner or later. Certain faults are common. Sores over the kyphos or crests are usually caused by insufficient padding. Small pieces of adhesive felt may not retain their position and the adhesive surface may cause irritation. The degree of hyperextension obtained has sometimes been quite inadequate, while some jackets, otherwise excellent, have been completely spoilt by trimming the pubic region too high. A few have buckled, especially those made too economically with Cellona or with large abdominal windows.

In all cases requiring hyperextension jackets, I use the Watson-Jones position, with the patient's own bed as the lower table. A sling of three-inch canvas webbing padded for the axillary regions and suspended by blocks and tackle has been found of great use in reducing the strain on the shoulders. The sling rides so high in the axilla and over the suprasternal notch that there is no interference with the application of the sternal plate. With its assistance the patient is easily swung round into position. Obese patients and cases of injury or amputation of the upper limb are comparatively comfortable during the unhurried application of the cast. Patients with fractured ribs do not find the cast an efficient splint, and the usual strapping fixation is an important preliminary. Fractures of the lower limb can usually be made comfortable for the necessary fifteen minutes by temporary fixation in plaster. The radiological pictures after the further application of jackets have been disappointing, as reduction is increasingly difficult to obtain or improve after the first week.

Our hospital material has not been suitable for a fair trial of the method of tidal drainage of the bladder in cases of paraplegia, as urinary sepsis and some degree of uræmia have frequently been present and suprapubic cystostomy was carried out as an urgent measure. So far there have been no regrets after suprapubic drainage. In males with urinary sepsis already present, tidal drainage has had to be discontinued on account of urethral inflammation; in females œdema of the vulva may develop after some weeks. Suprapubic drainage makes little difference to the treatment from the orthopædic point of view. Soiling of a plaster bed can be completely avoided, and if the tube is inserted one and a half inches above the pubic crest a plaster jacket can still be applied with the tube coming out through a small abdominal window.

Section of Physical Medicine

President—JOHN COWAN, M.B.

[*April* 26, 1941]

Electro-Diagnosis and Electrotherapy in Peripheral Nerve Lesions

By P. BAUWENS, M.R.C.S., L.R.C.P.

MUSCLE testing is a valuable aid to diagnosis in nerve injuries. The aim of muscle and nerve testing should be to obtain a quantitative estimation of the proportion of normal to denervated muscle fibres.

Polarization and allied phenomena play an important part in the passage of electric currents through tissues and on these we depend for the initiation of nerve and muscle responses.

When an electric current passes through an electrolyte, it does so by virtue of a migration of ions in opposite directions; these ions have dimensions and masses of the same order as those of atoms and molecules and they are therefore subject to hindrance by mechanical obstructions. Consequently, if a permeable membrane is interposed in the path of a current passing through an electrolyte, ions of opposite polarity will collect on either side of the membrane and exert an E.M.F. which will have a repelling effect on the oncoming ions of the same polarity (fig. 1). As this back E.M.F. of polarization comes into being as the result of the flow of current, it is clear that it does not exist at the inception of the flow. The initial current will therefore be greater than when the back E.M.F. which opposes it is established.

When an interrupted current of constant E.M.F. is applied by means of non-polarizable electrodes to the body, the skin acts as a polarizable membrane and even though the voltage wave be rectangular in shape, the current wave is not. It assumes the shape shown in fig. 2 (*a*). With a circuit affording an external path for depolarization currents, a current in the reverse direction can be detected at break as shown in fig. 2 (*b*).

If, on the other hand, the current is controlled by a diode or a pentode valve so as to keep the current of constant value, the E.M.F. across the patient assumes a wave which is not rectangular (fig. 3).

Polarization occurring at the level of the skin is of importance in muscle testing because, as can be deduced from the foregoing diagrams, it materially modifies the wave form of the stimulus.

In the deeper tissues, polarization also occurs wherever the ions responsible for the transmission of the electrical energy are slowed down and bank up, but this is not of great importance except inasmuch as the E.M.F.s of polarization set up currents in opposite direction at break, and these, when of sufficient intensity, act as a stimulus and produce contractions at break of the current.

From the point of view of excitable tissues, ionic movement in the body is of great moment, because under certain conditions it effects depolarization of naturally polarized tissues.

In nerve fibres at rest, there exists a difference of potential between the axis cylinder and the outer surface of the fibre. The fibre is said to be polarized—positively on the outside, negatively on the inside. Nervous impulses are accompanied by a zone of depolarization which travels down the fibre with them. Furthermore, artificially produced depolarization will initiate a nervous impulse.

Let us now consider the way in which an electric current applied to the body affects one nerve fibre when the current adopts a path co-axial to the fibre.

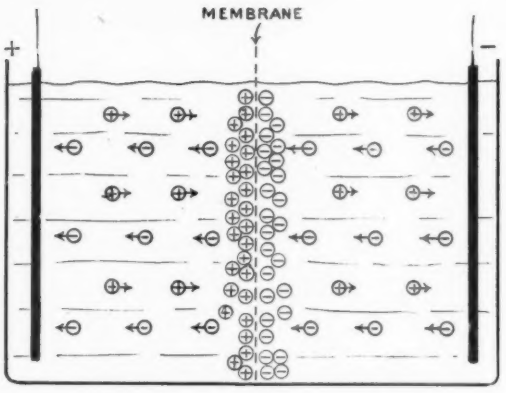


FIG. 1.—A permeable membrane across the path of an electric current in an electrolyte results in the banking up of ions of opposite charges on either side of the membrane setting up back E.M.F.s of polarization.

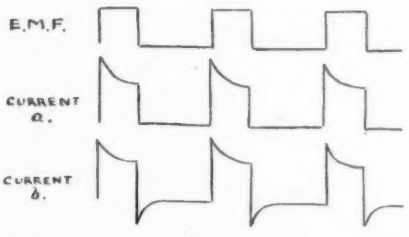


FIG. 2 (*a*).—An E.M.F. of rectangular wave form impressed on a polarizable load produces a current which has a high value at make but decreases as the result of the back E.M.F. of polarization partially opposing the flow. (*b*) A momentary current of depolarization flows in the opposite direction when a path offers itself at break.

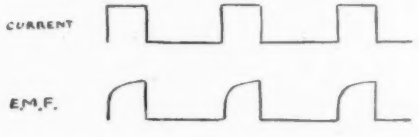


FIG. 3.—When the current in a polarizable load is of rectangular wave form, the E.M.F. across it reaches its full value after a delay.

In fig. 4, A and B represent a non-polarizable anode and cathode, while C D represents a nerve fibre at rest with a positive potential on the outer surface, and a negative potential on the axis cylinder, separated by the insulating myelin sheath.

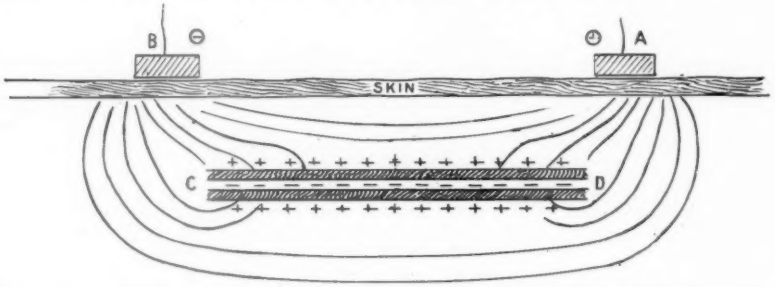


FIG. 4.—Currents in tissues can be transmitted in two ways: Solely by ionic connection in intercellular fluids and by a combination of this and displacement at the level of insulating membranes such as myelin sheaths.

At the instant when the circuit is closed, two paths are open to the current, a permanent one in the intercellular fluids, and a momentary one along the axis cylinder. The momentary nature of the current passing along the axis cylinder results from the presence of the myelin sheath with its insulating properties.

As can be seen from fig. 5 and the substitution diagram accompanying it, this momentary component of the current tends to depolarize the nerve fibre under the cathode—by neutralizing the positive surface charge—while it increases the polarization under the anode. If this depolarization under the cathode is adequate, a nervous impulse originates and this travels up and down the nerve with the accompanying depolarization wave. The latter may, however, be blocked at the level of the excessive polarization under the anode.

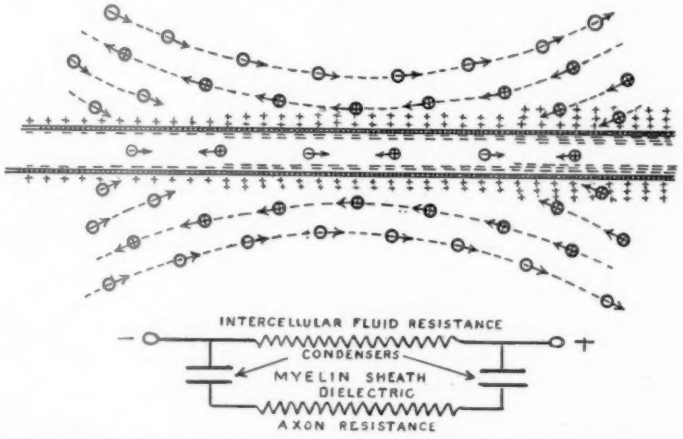


FIG. 5.—The natural polarization of the nerve is neutralized under the cathode and increased under the anode as the result of co-axial passage of an electric current through tissues.

In order that a nerve fibre may be stimulated in this manner, certain conditions have to be satisfied. The polarization of a nerve is not comparable to a static charge which, once neutralized, remains neutral. It is on the contrary constantly being regenerated and

for this reason, both time in regard to duration of flow, and intensity of current become important factors in electrical stimulation.

I shall not dwell on the well-known work which Dubois-Reymond, Hoorweg and Weiss did in this connection except to mention that their labours culminated in the intensity-duration curve which is the excitability characteristic of a nerve fibre. Fig. 6 is such a curve. The intensities required to cause a minimal response are measured along the ordinate for durations of flow of current measured along the abscissa. It is immediately evident that a minimum current is required in order to produce any reaction at all and this is termed the rheobase. When the duration of flow is materially shortened an additional amount of current must be used which is itself a function of the duration.

This involved sentence can be expressed by the formula:

$$I = \frac{a}{t} + b$$

where I is the current necessary to produce a response, *b* the rheobase, *a* a quantity of electricity which when divided by *t*, the duration of flow, becomes an intensity. Both *a* and *b* are constants for a given nerve or muscle and it was found that the ratio $\frac{a}{b}$ was itself a constant characteristic of its excitability. It will be seen later that this is the chronaxy and is indeed a time factor.

To measure the rheobase *b* it is merely necessary to find the current required for a minimal response when the duration is of the order of a second. This makes *t* large and therefore $\frac{a}{t}$ becomes negligible in the equation, and I then equals *b*. Having found the value of *b*, if we now find the time during which the current has to flow when the current used is 2 *b* our equation becomes

$$2\,b = \frac{a}{t} + b$$

$$\text{or} \quad b = \frac{a}{t}$$

$$\text{or} \quad t = \frac{a}{b}$$

In other words we find that when we use a current double the rheobase the duration of flow required for a minimal response is the ratio $\frac{a}{b}$ or chronaxy. The latter is expediently expressed in milliseconds.

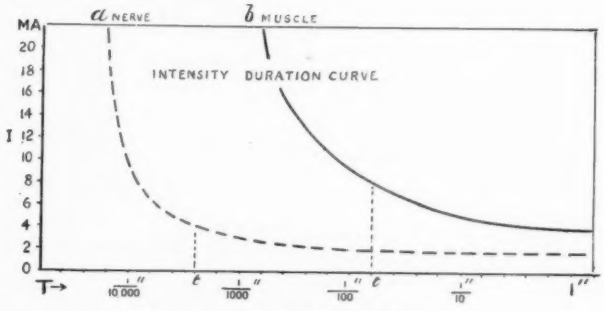


FIG. 6.—For explanation see text.

As a general rule, condenser discharges are employed in order to obtain the short durations necessary for chronaximetry. With this method the current wave follows an exponential law (fig. 7*a*). The apparatus which I designed and employ gives rectangular current waves (fig. 7*b*).

In this machine the current which passes through the patient is controlled by a pentode valve which has the advantage of making the wave-producing circuit independent of variations in the load, while the current output is unaffected by polarization in the patient or

by his resistance. Whether this has advantages over condenser discharges is debatable. It certainly allows one to ignore a number of inconstant factors. At the same time it should be remembered that the E.M.F. set up across the electrodes is not built up instantaneously. This may explain why French authorities working with ballistic or other rheotomes did not obtain results fully comparable with those obtained with condenser discharges.

The intensity-duration curve is the characteristic of excitability of one nerve fibre or muscle fibre, for in all work on electrodiagnosis it is essential to accept the unit concerned in this investigation as consisting of one nerve fibre and the few muscle fibres it supplies. The anatomical nerve and muscle is merely a complex consisting of a large number of such units grouped to perform a specialized mechanical function.

Referring again to fig. 6, which represents two widely different intensity-duration curves, *a* might be that of a normal muscle fibre and *b* might well be that of a fully denervated fibre. It follows that when a motor nerve is completely severed, each individual muscle fibre supplied by it will pass from a normal condition expressed by the characteristic

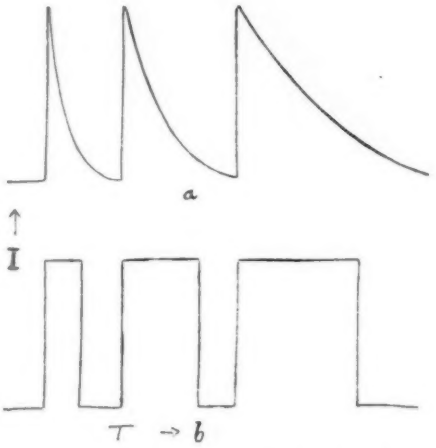


FIG. 7.—Wave forms of stimuli of varying durations suitable for chronaximetry. (*a*) Exponential—produced by condenser discharges. (*b*) Rectangular—produced by special valve controlled apparatus.

curve *a* to the abnormal condition characterized by curve *b* and will do so by way of a number of intermediate stages. As nerve fibres are of different lengths, it is doubtful whether analogous conditions obtain throughout the muscle at any one time during the transitional period. From a practical point of view, in case of complete anatomical or physiological interruption of nerve supply, the chronaxy soon passes from its normal value for the muscle under consideration to that corresponding to reaction of complete degeneration, which may be 100 times greater. The well-known absence of reaction to faradic stimulation and typical qualitative alterations in the response to galvanic stimulation which accompany this are too well known and too well understood to require reiteration here.

In the circumstances just described where homogeneity exists, interpretation presents no difficulty. The picture is entirely different when an incomplete nerve lesion is investigated.

For instance, when partial motor nerve injury occurs, after an interval the muscle supplied by it consists of a number of normal fibres interspersed with denervated fibres, each with its own characteristic excitability curve. To grasp the full meaning of the reaction to electrical stimulation of such a complex organ, we must realize that every ratio of the two types of fibres can occur and that as one increases the other decreases. To make this

point clear, I have drawn a number of hypothetical curves representing various possibilities ranging from 100% normal to 100% denervated with four intermediate stages (fig. 8).

Line A represents the intensity-duration curve when the muscle consists of normal fibres only. (The rheobase is 2 ma. and the chronaxy $\frac{1}{8000}''$.)

Line B represents the intensity-duration curve of the 80% normal fibres. It will be noticed that the rheobase has of necessity risen to 4 ma., but that this has in no way altered the chronaxy, which is still $\frac{1}{8000}''$. But with this 80% normal fibres there are mixed 20% fibres which have a completely degenerated nerve supply. The curve which these fibres with their increased chronaxy contribute to the picture is represented by the dotted line B^1. The full lines C, D, E and the dotted lines C^1, D^1, E^1 represent conditions where 60%, 40% and 20% normal fibres are mixed with 40%, 60% and 80% denervated fibres respectively.

Line F might be the intensity-duration curve of the muscle when it consists of 100% denervated muscle fibres. It will once more be noted that although the rheobase varies, the chronaxy is either that of the normal fibre $\frac{1}{8000}''$ or that of a completely denervated fibre $\pm \frac{1}{40}''$.

How is it then that intermediate measurements alleged to be the chronaxy are obtained in partial lesions? For the answer to this question we must see how chronaximetry is affected by two corresponding curves.

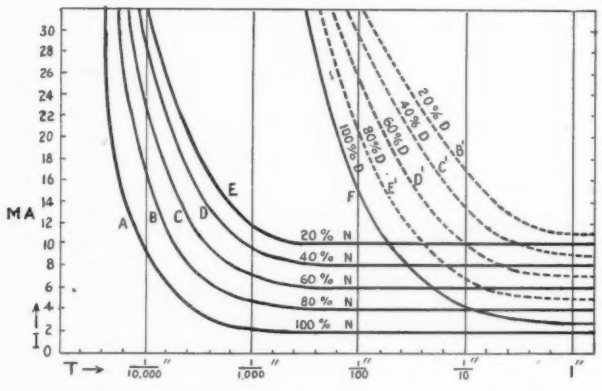


FIG. 8.—For explanation see text.

It is evident that when we are dealing with 100% normal or 100% denervated fibres, we obtain true chronaxy measurements. With curves representing 80% normal and 20% denervated fibres we shall obtain a normal chronaxy because we are in this case measuring the rheobase and chronaxy of the same fibres. The same applies in regard to 60% normal and 40% denervated fibres. But where we are dealing with 40% normal with 60% denervated fibres, the rheobase measurement is that of the denervated muscle fibres which is the lower of the two (7 ma. as compared with 8). When we estimate the minimal duration which will give a response with double this rheobase (14 ma.) we find we are stimulating the normal fibres and obtain a reading which is greater than the normal but which cannot be said to be the chronaxy of the muscle, as is held by followers of Lapicque and Bourguignon.

The same applies to an even greater extent in the condition existing where 20% normal fibres co-exist with 80% denervated fibres; the pseudo-chronaxy here being about $\frac{1}{800}''$.

It is of interest to note that out of all the curves I used to illustrate my point only two give intermediate readings. Admittedly these curves are imaginary but they serve in a measure to explain why such readings are uncommon except where degeneration or regeneration is in progress when a large proportion of the actual chronaxies of the muscle fibres

are in a state of flux. It also shows how chronaximetry if taken at its face value can be misleading.

Other quantitative methods of assessing the extent of a nerve lesion from electrical exploration of the muscles have been attempted and mention should be made of that utilizing the discharge of condensers of various capacities charged to a constant potential. In skilled hands and with the full appreciation of its pitfalls this technique may be of value. However, the impedance through which a condenser discharges varies the rate of discharge or current, and also the duration of the discharge. Since the body with its variations of resistance at the level of the skin and of conductivity in the deeper tissues is anything but a constant as an electrical load, it follows that this becomes a way of making a rough estimation only. If we examine closely the shape of a condenser discharge such

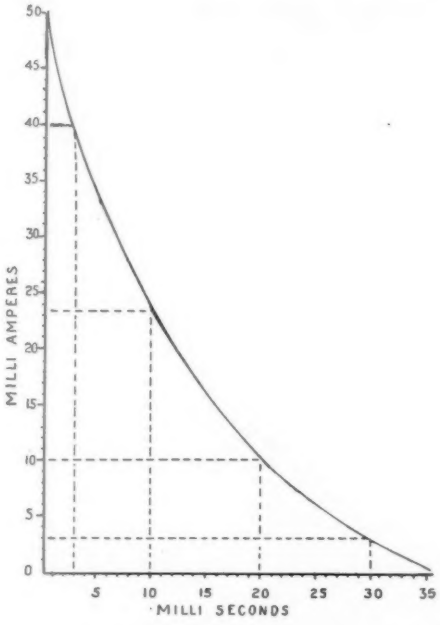


FIG. 9.—A condenser discharging according to an exponential law may stimulate tissues with different excitability characteristics.

as is represented by fig. 9 we at once note that a current with such characteristics is capable of stimulating nerves and muscles with widely different requirements as regards intensity and duration. The hypothetical curve under consideration would stimulate muscles requiring 40 ma. for $\frac{3}{1000}$", 23 ma. for $\frac{1}{100}$", 10 ma. for $\frac{2}{100}$", or 3 ma. for $\frac{3}{100}$".

With rectangular waves, this objection no longer holds, and the solution to the problem may well be in the employment of such waves. I do not suggest that a whole intensity-duration curve should be plotted for each muscle investigated, but that three points be selected, one corresponding to about $\frac{1}{1000}$", that is of the order of that of faradic currents —another of a duration of approximately $\frac{1}{10}$" and an intermediate one. The relationship of currents required to obtain a minimal response with these three time values should give a better idea of the condition of the nerve than chronaximetry. For comparison's

sake it would be expedient to reduce the rheobase to unity. For example, if the readings obtained were:

2 ma. for $\frac{1}{10}$" duration
4 ma. for $\frac{1}{100}$" duration
8 ma. for $\frac{1}{1000}$" duration

then taking 2 ma. as the rheobase, the readings would have to be recorded as 1 - 2 - 4, or even 2 - 4 since the first figure would invariably be unity.

This would not be so far removed from the classical method of testing with faradic and galvanic currents with which only two points on the curves are explored, one of which —that corresponding to the duration of the faradic impulse—is not easily measurable.

The correct technique of muscle testing is of importance, particularly the inclusion of a test of nerve conduction wherever possible, both with faradic and galvanic impulses. The ulnar nerve and median nerve can be stimulated at the level of the elbow and the wrist; the external and internal popliteal nerves at the level of the knee-joint; the posterior tibial nerve behind the internal malleolus. In brachial plexus injuries, useful information may be gleaned from stimulation of the upper trunk of the plexus which is easily found in the supraclavicular fossa. The middle trunk is not so easily stimulated.

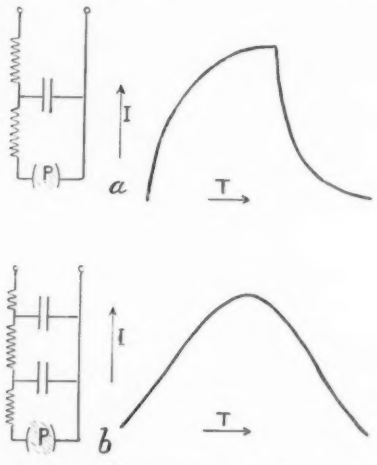


FIG. 10.—Condensers connected in parallel with a load, delay the establishment of the full current. (*a*) Wave form when one condenser is employed. (*b*) When two condensers are employed.

So far, I have only dealt with problems relating to a single exploration, which is really of no more value than the isolated reading of a thermometer. Far more information can be gathered from a chart. This is equally true of muscle testing. If one had the opportunity of examining the patient carefully every two or three days for three weeks following the injury, the rate at which alteration in responses to electrical stimulation occur would constitute valuable data. Unfortunately we are too often faced with old-standing cases in which it is difficult to obtain even a galvanic response without stimulating the surrounding normal muscles, and in which exact muscle testing is sheer waste of time. In many ways the same applies to the continued muscle testing where reaction of complete degeneration has existed for some considerable time; for if complete anatomical or physiological interruption has occurred and regeneration has yet to occur, the voluntary control will return before measurable changes can be assessed electrically. Here I wish to make a qualifying statement as regards nerve stimulation for I have often been able to demonstrate a muscle response by stimulating the nerve trunk with currents

of long duration, where the muscles themselves still exhibited reaction of complete degeneration and chronaxies corresponding to complete degeneration.

My theory is that this can be explained by assuming that the young axon grows down a very imperfect sheath wherein the normal polarization of the nerve fibres is defective or non-existent. In such a case it would be impossible to stimulate the unpolarized nerve fibres below the site of the lesion with currents of short duration, although conduction might be possible along the axon. In fact we would have absence of excitability of the nerve in the presence of conduction. A somewhat similar state of affairs appears to exist in the muscles themselves. The regenerating nerve fibres are not excitable and therefore responses are obtained only by direct stimulation of muscle fibres with currents of long duration. It is, however, notable that in normal muscle it is possible to excite the muscle fibres directly by using, as Lapicque pointed out, currents which instead of reaching their maximum value instantaneously, do so gradually. Retardation of onset can be brought about by connecting condensers in parallel with the electrodes used on the subject. The E.M.F. across the condensers and electrodes will rise at make and fall at break according to a curve shown in fig. 10 (*a*).

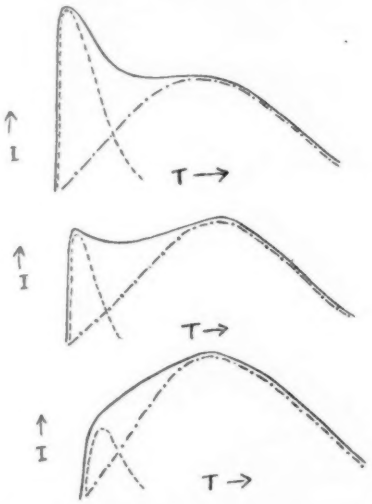


FIG. 11.—Under conditions of partial nerve lesion, responses obtained (full lines) may be the integration of the brisk reaction of normal muscle fibres (broken lines) coupled with the sluggish reaction of denervated muscle fibres (dot-dash lines).

When two condensers in cascade are employed an E.M.F. curve similar to the one shown in fig. 10 (*b*) is obtained. In both cases, however, the currents are greatly affected by the resistance of the patient.

When a progressive current such as the one described is applied longitudinally to a normal muscle there is a considerable discrepancy between the current required to stimulate the muscle with this and with a rectangular wave, the ratio being of the order 1:4 whereas in denervated muscles, the ratio is of the order 1:1·5 or 1:1.

It is difficult to explain such a lowering of the threshold to progressive currents without postulating that changes in the excitability of the muscle fibres themselves occur when the axons degenerate. Indeed it would appear that the fibres regress to an excitable state similar to that of unstriped muscle. Such an alteration would account for a number of otherwise perplexing facts such as the sluggish response sometimes obtained when the nerve trunk or the motor point is stimulated with faradic impulses, and the persistence of enormous chronaxies long after apparently total functional recovery.

To epitomize ; we have at our disposal five methods of exploring the extent of nerve damage.

(1) *The classical method* in which nerve trunks, motor points and the muscle itself are stimulated in turn by faradic and galvanic currents. Simplicity of apparatus and of technique commend it. Unfortunately the faradic current cannot be measured. The galvanic current can be measured but the values are of little significance. Of greater value are the qualitative features of the responses obtained. It must be remembered that this response may be the resultant of two contractions when the muscle tested consists of mixed fibres—normal and denervated. The former will account for the brisk component at make, the latter for the sluggish contraction which gives the impression of slow relaxation. Naturally the ratio of the two types of fibres will determine the overall response. Fig. 11 shows how the integration of a normal muscle response and a sluggish one gives a response with a brisk inception and slow relaxation. Where pain makes it impossible to use currents of sufficiently high intensity to be conclusive, an anæsthetic may be resorted to.

(2) *Chronaximetry* is exact only when all nerve fibres undergo degeneration or regeneration at the same rate and where homogeneity exists. It fails to reveal the presence of normal fibres. This is particularly the case when rectangular wave impulses are used although it may do so when exponential condenser discharges are used.

(3) *The Cluzet method,* which was also adopted by Lewis Jones, is almost certain to detect normal fibres, since condensers are charged to a definite potential and strong impulses of short duration are always started with. But here the shape of the stimulating current curve is dependent on unpredictable factors such as skin resistance, œdema, &c. Moreover there is, as pointed out before, the possibility of stimulating various fibres simultaneously with exponential stimuli.

(4) *Plotting an intensity-duration curve,* employing rectangular waves. This technique would be most tedious and nearly as much information can be reaped from a curve plotted from three points representing three different durations—the base line being reduced to unity.

(5) *By means of modulated currents.*—To stimulate a nerve the onset of the current must have a steeper gradient than to stimulate muscle—particularly denervated muscle, and the ratio of the current required to stimulate a muscle with rectangular waves to that required to stimulate it with a progressive current bears a relation to the state of the muscle and nerve.

The investigation may be carried out with a bipolar or longitudinal application of electrodes.

Each method has its advantages in certain circumstances. The faradic current will reveal the presence of normal muscle fibre except where considerable œdema is present, while the progressive currents will pick out denervated fibres. Chronaximetry, by detecting early return towards shortened chronaxies may point to concussion of the nerve as opposed to more severe damage. Galvanic stimulation of the nerve trunk may indicate recovery before voluntary control has returned.

With regard to the value of artificially produced muscle exercise in paralysis, on the assumption that function improves the organ, I believe in electrical stimulation of paralysed muscles, for although it does not prevent atrophy, circulation and nutrition are improved. To be effective and non-injurious it is important to use a technique which will not produce contractions in normal muscles surrounding and opposing the paralysed ones. Fatigue must be avoided by allowing long pauses of rest between contractions which should be few in number. If the blood supply is inadequate this treatment may have to be withheld.

Where interrupted galvanic currents produce contraction of antagonistic muscle groups, the progressive currents or modulated direct current should be used.

Section of Therapeutics and Pharmacology

President—Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P.

[*May* 13, 1941]

WALTER ERNEST DIXON MEMORIAL LECTURE

[Number 3]

Sir William Willcox in his opening remarks gave an outline of the origin and history of the W. E. Dixon Memorial Lecture. He welcomed the presence of Mrs. W. E. Dixon and introduced the third Dixon Lecturer, Professor J. A. Gunn, who had chosen as the subject of his Lecture "The Future of Pharmacology".

The Future of Pharmacology

By J. A. Gunn, M.A., M.D., D.Sc., F.R.C.P.

Nuffield Professor of Therapeutics in the University of Oxford

Summary

[This lecture takes up the criticisms, made by Professor Dixon in his Presidential Address to the Section of Physiology of the British Association in 1929, that in Great Britain pharmacology is the most neglected branch of medicine, that the practical aspects of the subject are insufficiently accentuated and that British pharmacology is so much behind that of other countries in the production of new remedies. An account is given of the trends of progress in pharmacology since this Address. The main development has been the increased scope and intensity of research devoted to the discovery of new remedies among synthetic compounds. Such investigations demand the co-operation of pharmacology with synthetic chemistry and with bacteriology; and medical schools should endeavour to provide adequate support and facilities to their pharmacological laboratories so that they may take a substantial share in these advances. Otherwise the search for new remedies may be left to commercial laboratories and this is more likely to happen if academic laboratories devote themselves too universally or exclusively to specialized pharmacology.

The lecture shows how the scope of pharmacology has so widened and its relations with cognate sciences become so diversified that it is no longer possible to regard it merely as a branch of physiology. Its progress will be hampered unless it has the status, both for research and teaching, of a separate discipline, requiring its own staff, accommodation and resources. It is pointed out that the value of chemical agents in the treatment of disease is being established on a broader and sounder foundation and that this knowledge is too important in the practice of medicine for it to be left to indeterminate supervision.]

I wish first of all to thank the Council of the Royal Society of Medicine for the honour they have done me in inviting me to give the W. E. Dixon Memorial Lecture. As one

who co-operated with Dixon in many activities which concern the welfare of pharmacology and who enjoyed close friendship with him for so many years, I regard this invitation both as a privilege and as a responsibility.

Dixon had a twofold interest in pharmacology. He was in the first place an investigator, occupied with research in pharmacology and in the elucidation of its problems. The part he played in advancing knowledge I have already attempted to assess (*J. Pharmacol.*, 1932, **44**, 1), and, as time goes on, his individual contributions will merge into the general corpus of knowledge. I wish only to add in this connexion a quotation from the first of the Memorial Lectures delivered by Sir Henry Dale (*Proceedings*, 1934, **28**, 319): "Nobody who looked at this list (of his publications) can fail to be struck by the wide variety of subjects on which he worked and wrote. His researches were characterized by range and variety rather than by intensive and deep exploration in a limited field." This lecture is, in fact, partly a plea for the recognition of the necessity of pharmacological research in range. This is not to disparage research in depth, which is, from many points of view, the most interesting and attractive side of pharmacology, as of all sciences, but there must be a sufficiency of range as well. Dixon was, in the second place, interested in the scope and function of pharmacology as a subject, its place in the medical curriculum, its importance in medical practice as a basis for scientific therapeutics and the facilities, academic or other, that should be given to it, so that it could best fulfil these functions. I wish also to refer to this second interest, because there have been for some years past misgivings, especially perhaps in this country and in America, as to the necessity for pharmacology as a separate discipline, both for research and teaching, in medical schools.

In one of his last public lectures, that which he gave as President of the Section of Physiology of the British Medical Association at the Meeting in Cape Town in 1929 (*Brit. Med. Journ.*, 1929 (ii), 138), Dixon expressed dissatisfaction with the position of pharmacology in this country and with its lack of therapeutic outlook in research. Some idea of his criticisms can be got from the following excerpts from his Address:

"It may be argued that the body of a living man is a machine, the actions of which are explicable by the known laws of physics and chemistry: and that, therefore, the correct way to study physiology is by applying these sciences to the cell. I am by no means averse to the vast amount of academic research on these lines which is published annually, often by workers with little biological knowledge or training, but it surely should not precede the more immediate practical aspects of the subject. The modern attitude is expressed by a young biochemist who in reviewing a well-known book on chemotherapy in 1928, asks 'might not the time and resources spent on chemotherapeutic research be diverted more profitably to the study of chemical and physical mechanisms?'"

"No branch of experimental biology has received less consideration in great Britain than that of pharmacology. It is also the most neglected branch of Medicine."

"From what has been said, it is not surprising that British pharmacology should be so much behind that of other countries in the production of new remedies; practically all come from abroad."

It is now more than a decade since Dixon delivered the Address from which I have quoted. What has happened in the interval? Is pharmacology still the "most neglected branch of medicine?" Are "the more immediate practical aspects of the subject" still being overlooked? Is British Pharmacology still "so much behind that of other countries in the production of new remedies?"

Reorientation of Pharmacology since 1870

When, about the middle of last century, pharmacological research reached sufficient volume and intensity to matter, the *materia medica* consisted mainly of plants and inorganic compounds. Their medicinal use was based upon tradition and empiricism. In few cases could a scientific explanation be given of the way in which they acted and in many cases there were serious doubts as to whether they produced any effect at all. Thus it was right and natural that pharmacological research should devote itself to the examination of the credentials of this heritage of drugs. Early pharmacology, therefore, concerned itself mainly with the investigation of the action of drugs which had been empirically introduced into therapeutics.

It was a natural corollary to this work to investigate plants or inorganic substances which had only tentatively, if ever, been employed as medicinal agents. A fruitful example of this class of investigation was Fraser's work, published in the decade 1860-70, on the "characters, actions and therapeutic uses of the Ordeal Bean of Calabar". This work was in the best style of early pharmacology, a careful investigation of the actions of calabar bean according to the experimental methods then available. It was an investigation of a plant that hitherto had been known only as a poison. It revealed novel and interesting physiological actions and it led to a new and important addition to practical therapeutics.

Numerous papers still appear dealing with facets in the pharmacology even of the oldest known alkaloids, like morphine and strychnine. Indeed it is difficult to conceive of the pharmacology of such energetic substances being complete in the sense that nothing of interest remains to be added to it. Many new plants have also been investigated and a few of these have provided new and valuable remedies. The decade (1860-70) saw, however, the publication of the results of two pharmacological investigations which were destined, powerfully and permanently, to alter the orientation of pharmacological research by revealing the possibilities of the pharmacological and therapeutical value of artificially made, as opposed to naturally occurring, substances.

The first of these investigations was that by Crum Brown and Fraser: "On the connexion between Chemical Constitution and Physiological Action." This opened up for pharmacology a vista which has at times appeared to be the dawn of a new day, at times only a will-o'-the-wisp. Though the factors are too complicated to enable a sure prediction to be made of the pharmacological action of a compound from the mere consideration of its chemical structure, nevertheless the search for such relations has given an impetus to pharmacology. Apart from the incidental discovery of new remedies through this type of inquiry, the modification of physiological action produced by change in chemical constitution provided one avenue by which an approach could be made towards the understanding of more fundamental problems of pharmacology, e.g. the chemical or physical basis for pharmacological activity. Such investigations almost always entailed, however, the synthesis of new compounds of a chemically homologous series. They demanded the assistance of synthetic chemistry.

The second investigation was that by which Liebreich (1869), looking for new anæsthetics allied in constitution to chloroform, discovered the hypnotic action of chloral. The general anæsthetics, ether, chloroform and nitrous oxide, had been discovered about twenty years earlier but the discovery of the hypnotic action of chloral, though intrinsically less important than that of the general anæsthetics, more positively suggested a therapeutic future for new synthetic compounds. As a chemical substance, chloral had been discovered by Liebig in 1832, and for over a third of a century medicine had been deprived of a useful remedy for the lack of pharmacological investigation. The moral was obvious. More pharmacological research should be devoted to artificial compounds.

From such beginnings, a significant change has come about in the distribution of pharmacological research, in that there has been a proportionately far greater increase in the volume of research devoted to the investigation of artificial compounds. After the publication of the last edition (1932) of the British Pharmacopœia, I prepared an analysis (*Pharm. J.*, 1933, p. 76) showing the number of substances and preparations in each of six groups of drugs included in successive British Pharmacopœias from 1864 to 1932. Among the conclusions reached were the following: "The number of plants mentioned has diminished in that time (since 1885) from about 170 to less than 100. The number of plant galenicals in the B.P. 1932 is less than half of that in B.P. 1885. The number of inorganic substances and their preparations has declined with almost equal rapidity. The group of vegetable active principles and their preparations and that of preparations from animal sources have remained almost stationary in number. The only group to show a steady absolute increase in number is that of synthetic remedies."

Pharmacopœias can be taken to reflect, conservatively, the tendencies of pharmacological and therapeutic progress and there is evidence that, since 1932, the number of remedies of artificial origin has still further increased, both absolutely and relatively. It is significant, for example, that in the Third Addendum to the B.P. issued in the beginning of this year, of the 17 new additions to the Pharmacopœia, 16 are synthetic compounds or preparations of them.

This brief retrospect shows that, although pharmacological research still concerns itself with the deeper analysis of the action of known and naturally occurring active principles and also with the examination of the diminishing number of hitherto untested plants, the great bulk of pharmacological research, in so far as it seeks to advance therapeutics, is now occupied with the search for new remedies in the unlimited field of artificial compounds. This change in the distribution of pharmacological research has had effects which have not been sufficiently realized. Especially has it involved quantitative changes in the relationships of pharmacology with the sciences to which it is most intimately related, and a brief consideration of these relationships may help to clarify the position.

Relations of Pharmacology with Synthetic Chemistry

The preliminary qualitative investigation of the pharmacological activity in a plant can in many instances be made, up to a point, with relatively simple chemical apparatus and without highly specialized chemical skill. The existence and type of action of calabar bean or of strophanthus could be shown by examination of their extracts. Once an interesting pharmacological property was discovered, the isolation of active principles and especially the determination of the chemical structure of such principles was of direct interest to the pure chemist. This was, in fact, one of the primary problems of organic chemistry. There was, therefore, every prospect that this side of the inquiry would be dealt with by the organic chemist. The problem had a proved practical value as well as a theoretical interest.

When we come to the modern search for new remedies, which usually involves the preparation of many compounds of a homologous series, the conditions are rather different and neither of these stimuli may exist. The synthesis of a group of new compounds may possess little chemical interest since their preparation may involve only the application of known methods to new material. The work requires accommodation, plant, staff and finance and the academic chemist may well say that he has more important work to do with his limited resources. Moreover the pharmacologist cannot guarantee that the proposed compounds will have any new pharmacological properties or any real therapeutic value. Though an easy and obvious solution of the quest for new remedies would seem to lie in the co-operation of the pharmacologist and the organic chemist, this co-operation has, in fact, seldom materialized in academic laboratories.

It might be suggested that the answer is that a pharmacological laboratory ought to have its own chemical laboratory, capable of providing new compounds as required. In practice this is virtually impossible. It means the duplication (though on a smaller scale) of the accommodation, equipment, staff, &c., of an existing laboratory of organic chemistry. Naturally a University looks askance at such a proposal, even if it were financially possible, it being an added deterrent that such a laboratory would not necessarily play any part in the teaching of organic chemistry. Whether this be the sole reason or not, the fact remains that no University pharmacological laboratory in this country, so far as I know, possesses the chemical resources to prepare new synthetic compounds on a sufficient scale, and the scale needed for discovery of even an improvement over a compound of established therapeutic value must usually be extensive. Dr. Trevan has mentioned that to his knowledge, over 140 variants of sulphanilamide had been prepared without discovering one which was sufficiently superior to the existing compound to warrant its production. Since he made this statement a still greater number of related compounds have been synthesized and tested and of these perhaps not one in a hundred represents any therapeutic advance. The crucial point which is not sufficiently realized in medical schools, is that the search for new remedies among synthetic compounds involves chemical synthesis on a large scale. The field must be wide though it may not be ploughed very deep.

For a University laboratory to take up work of this kind is not an entirely encouraging prospect. The primary object of the research is utilitarian—the discovery of a new remedy, and the value of the work is apt to be assessed by its success in this direction only. The pharmacological skill and imagination devoted to the investigation of a group of compounds may be exactly the same, whether a new remedy is discovered or not, but, unless the pharmacologist discovers a new remedy, the work he has done remains merely an addition to knowledge of a group of compounds in which, since they find no place in therapeutics, few people have any interest.

Relations of Pharmacology with Physiology

Physiology concerns itself with the normal functioning of living organisms or tissues. Pharmacology deals with the modifications of function that are produced by chemical agents. The methods used in both sciences are largely the same. Pharmacological explanations must be based upon current physiological concepts. Professed physiologists have made important additions to pharmacology and, perhaps to a greater extent, professed pharmacologists have made addition to pure physiology. The subjects are so closely allied and the boundaries between the two so indefinite that it may seem unnecessary, or even unwise, to separate them. It is a question which medical schools have to answer. The question may be whether an existing chair and department of pharmacology should be continued or whether it is worth while creating them if a medical school does not already possess them. Though the methods employed by both sciences are largely the same, the primary aims and outlook of pharmacology are so different from those of physiology that they can best be regarded as separate disciplines requiring separate direction and accommodation. The reasons for this belief I shall give shortly from the point of view both of research and teaching.

The study of the modifications of function produced by chemical agents has been, and will continue to be, of great value to physiology. Chemical agents, like adrenaline and acetylcholine, may be normal constituents of the body, playing, as we now know, parts of outstanding importance in the normal functioning of the body. Their actions are intimately and legitimately part of physiology proper. The study of the action of other agents, like physostigmine, atropine or nicotine—not normal constituents of the body—has played an important part in advancing physiological knowledge. But the general pharmacology of these substances had first to be investigated before it was known that they possessed physiological action at all. Unless Fraser, or someone else, had described the type of action of physostigmine, this alkaloid would not have been available as a tool for the physiologist.

One can, in fact, almost divide the pharmacological investigation of a substance into two stages: (*a*) a description of its general pharmacological actions which will indicate what particular organs it acts on and how it influences them; if this investigation fails to reveal either any action that promises therapeutic value or some peculiarity of action that is of exceptional physiological interest, then it may be " uneconomic " to pursue the investigation farther, in view of the hundreds of compounds awaiting possibly more profitable investigation; (*b*) if the substance shows any action of therapeutic or physiological interest, this particular action can be more intensively and quantitatively analysed. This distinction between (*a*) the general, and (*b*) the particular, pharmacology of a substance is important. There are, first of all, certain drawbacks to general pharmacology. It involves a wide range of experiment rather than an intensive study of one system or organ. The toxicity of the substance has to be determined and the symptoms that it produces in the intact animal, after which a range of experimental methods must be employed, the variety of which will depend upon the nature of the pharmacological action of the particular substance. For general pharmacological investigation the pharmacologist therefore requires a wide training in physiological technique. The pharmacologist has to move from one type of experiment to another, relying on his experience and judgment in deciding how far it is economic to pursue the investigation in " depth ". He must have a competent knowledge of general physiology so that his pharmacological descriptions and explanations may correspond with the physiological concepts of his day and he must use methods which, if not necessarily the most elaborate known to physiology, are at least adequate. At the end of his labour he may find that the compound or compounds he is investigating show no actions of exceptional physiological interest or any actions likely to be of practical therapeutic value. In regard to the latter question, the substance must not merely show actions of potential therapeutic value but must have a therapeutic value in some way superior to any recognized and available remedy. As the number and variety of remedies increase, the satisfaction of the latter criterion becomes increasingly difficult.

As compared with investigations of general pharmacology, research in particular pharmacology offers certain advantages. If a worker confines himself to the study of the action of one or more drugs on one particular organ or system, he may require only one type of apparatus, he will certainly not require the spread of technique that is

necessary for general pharmacology. He can not only legitimately limit his technique but he can, without flaunting his ignorance, restrict his reading of literature which, with the vast increase in volume of physiological and pharmacological research, is becoming more and more exacting and time-consuming. As a consequence of the comparative attractions of general and particular pharmacology, men beginning pharmacological research usually show a decided preference for particular pharmacology, and often never leave it.

There are two important consequences of this tendency towards too exclusive particular pharmacological research. The first is that it involves early specialization. Whatever may be true of physiology, I am convinced that early specialization in pharmacology is a mistake. I am not alone in this opinion. A recent letter from an American colleague says: "Our chief job seems to be to get some sort of control over the tendency toward early and intense specializing." Beginners are apt to be obsessed by the amenities of specialized research and perhaps influenced by the glamour of some great scientist who had pursued investigation in "depth", forgetting that he almost invariably had begun with a wide training and had pursued investigation in depth only when he recognized that the time was ripe for it. In any case genius is a law unto itself, but, for the ordinary man, too early specialization in science is apt to lead to scientific sterility. In the second place, specialized pharmacological research may soon lose touch with therapeutics. For example, the action of concentrations of a drug on an isolated organ may be interesting from a physiological point of view although those concentrations may be many times greater than would occur in the blood even with a lethal dose of the drug. The investigation may possess physiological, but no longer therapeutic, value. The more "physiological" research in pharmacology becomes, the more hazy becomes the distinction between physiology and pharmacology and the more unanswerable becomes the contention of those who maintain that the work done in a pharmacological laboratory could be equally well done in a physiological laboratory. Moreover the search for new remedies, which becomes more and more the function of pharmacology, and the justification for separate pharmacological laboratories, is impossible without general pharmacological research, upon which in fact it must be founded.

It has been said that since the introduction of physostigmine and strophanthus—that is, for a period of over half a century during which time the number of academic laboratories has much increased—no new remedy of importance has emanated from a British academic pharmacological laboratory. This seems a poor record, but the explanation may be simply that the discovery of a new remedy usually necessitates a width of research greater than that which academic laboratories have felt called upon to undertake.

Relations of Pharmacology with Bacteriology

The scope of pharmacology in regard to outlook and technique has been still further extended in recent years by the growth and success of that branch of chemotherapy which investigates the remedial action of drugs on diseases due to micro-organisms. In so far as pharmacology is regarded as a branch of physiology and using the ordinary technique of physiology to determine the modifications of function produced by drugs, the resultant remedies tend to be used chiefly for the relief of the symptoms of disease; they are seldom directly curative, though relief of symptoms may aid and accelerate the natural processes which lead to restoration of health. For example, valuable though they are as remedies, adrenaline does not "cure" asthma, nor does digitalis "cure" cardiac disease. With diseases due to infection by micro-organisms, the problem is in some ways simpler in that the primary disease ceases when the infection ceases, though of course pathological changes may remain which offer further problems for therapeutics. The knowledge which has been acquired of the parasitic origin of so many of the most important diseases and the resulting effect on pharmacological conceptions and outlook have been, perhaps, the most important factors in securely establishing belief in the value of chemical agents in the treatment of disease.

Though some remedies of this kind, e.g. quinine for malaria or ipecacuanha for dysentery, were discovered empirically by treatment of naturally occurring diseases in man and long before the organismal origin of the diseases were known, the modern search for new remedies of this type, at any rate in its preliminary stage, is conducted mainly by experiments on laboratory animals. Investigation of this kind involves three factors: (1) The synthesis of new compounds; (2) the induction of the infection; and (3) the action of drugs.

The first factor requires the assistance of synthetic chemistry to which I have already referred. The second requires the assistance of bacteriology, for the organism must be isolated and cultured and the course of the disease and the pathological effects it produces must be known. Finally not only must the effect of the drug on the disease be determined but, before it can be used therapeutically, its acute and chronic toxicity, general actions and side actions, absorption and excretion, &c., must be investigated.

This work requires the co-operation of the bacteriologist and pharmacologist, unless one man can combine both disciplines. If the work is to be done in a pharmacological laboratory, it means the introduction of a certain amount of bacteriological technique. Usually large numbers of animals are required, sometimes of one particular species, and the cost of the investigation may be high. This aspect of pharmacological research brings pharmacology into closer relation with bacteriology than with physiology. It would be a serious defect if, through lack of co-operation or resources, academic laboratories failed to take a substantial share in this development of pharmacology. It is not necessary or even economic that every laboratory should undertake such investigations but they should not be left entirely to extramural or commercial laboratories. This work does, however, mean the abandonment of that restricted view which regards pharmacology merely as a branch of physiology.

Commercial Research in Pharmacology

In the meantime, however, outside academic walls, another development is taking place, begun in Dixon's time and acquiring increasing momentum; that is, the establishment of commercial pharmacological laboratories. This is a significant development, which, as it is occurring in most manufacturing countries, will probably be permanent, and which may, and probably will, affect the future of academic laboratories.

Drug firms, which previously, for example, prepared active principles or galenical preparations, have turned their attention to the search for new remedies among synthetic compounds. Partly owing to the difficulty of getting the compounds pharmacologically investigated in academic laboratories, some of these firms set up their own pharmacological laboratories. This happened first in Germany but other countries, especially Switzerland, United States, and Great Britain, followed suit, and now there are in many countries pharmacological laboratories attached to drug factories which for staff, accommodation, equipment and finance, equal or excel the corresponding provision that the Universities have been able to make.

The primary incentive of these laboratories was naturally the discovery of new remedies, by the sale of which the manufacturer hoped to recoup himself for the expenses of research, but many of the more liberally minded firms have not only permitted but encouraged pharmacological research of a purely scientific kind which offered no immediate prospect of commercial reward. Indeed, some of these laboratories have done, and are doing, important work of this kind.

When we turn back to Dixon's complaint that practically all new remedies come from abroad and that British pharmacology is much behind that of other countries in the production of new remedies, I think this has become diminishingly true so far as commercial laboratories are concerned.

Well-equipped commercial laboratories have been established in this country and there are indications that we are at least holding, if not gaining, ground, in comparison with other countries in the discovery of new remedies. It has taken two world wars to make us realize that it is dangerous for this country to be so dependent upon imported drugs, apart from the disadvantageous financial side of the question. There are possible drawbacks to the introduction of drugs from the commercial side. These have been clearly explained by Trevan in his Presidential Address to this Section (*Proceedings*, 1937, 31, 267) and need not be recapitulated here. It must be remembered that the therapeutic efficacy of a drug is not in the least influenced by the motives which inspired its discovery.

Some of the practical problems confronting academic pharmacological laboratories in their relation to chemistry, physiology and bacteriology have been mentioned. How far do the same difficulties affect commercial laboratories?

In regard to the supply of compounds for investigation, commercial laboratories are usually in an advantageous position. They may have a larger staff of chemists whose job it is to make the compounds, regardless of whether or not the syntheses are of much interest from the point of view of pure chemistry. They may have available, from othe-

branches of manufacture, intermediate products which save stages in the syntheses. They can usually make the compounds on a larger scale, as they have the requisite plant. They can make an amount adequate not only for pharmacological investigation but for subsequent therapeutic trials. From the physiological side they are prepared to investigate compounds in surface, primarily to see whether they offer therapeutic promise or not. From the chemotherapeutic side, they can restrict themselves to one or more infections in which they are interested, with a corresponding saving in technique and material, whereas an academic laboratory, if only from the point of view of teaching, must take a much wider interest in bacteriology. Finally the financial resources of a commercial laboratory may be greater than those of academic laboratories.

It would seem, therefore, that, in the search for new remedies, commercial laboratories may be, both in regard to volume and speed of research, in a more favourable position than academic laboratories, and it is significant that, in fact, most of the new remedies which are being introduced have come in the first instance from commercial laboratories. It may have serious consequences if the search for new remedies is confined to commercial laboratories and if academic laboratories take little or no share in it. If the latter restrict themselves too much to particular pharmacology, academic research may easily become more and more physiological and less and less concerned with advances in therapeutics, and thus may easily afford justification for the abandonment of separate pharmacological laboratories in medical schools and the merging of them in the department of physiology.

The Teaching of Pharmacology

I wish now to proceed to the question of how these considerations affect the teaching of pharmacology in medical schools and its position in the medical curriculum. A few years ago there was issued a Report of a Conference of representatives nominated by the Universities of Oxford, Cambridge and London and by the Royal Colleges on the Medical Curriculum. The conclusions arrived at by this conference may be regarded as a representative and authoritative modern view. Here are the recommendations in regard to pharmacology:

"The Conference has considered the place of pharmacology in the Curriculum and the desirability of a separate examination in this subject. This subject is intimately connected with experimental physiology and much of the practical pharmacology course might be carried out in a department of physiology. A knowledge of the physiological action of drugs is, however, of primary importance to the student and the Conference believes that a short course of lectures and practical work on this subject is essential. Whether such a course should be given in the department of physiology or in a separate laboratory of pharmacology is a question to be settled in the different teaching schools. The Conference recommends that there should be no separate examination in pharmacology and believes that a knowledge of this subject should be tested either by the inclusion of pharmacological questions in the physiology paper and in the practical examination or by a viva-voce examination.

"The Conference is of opinion that a knowledge of doses should not be required from a student before he begins his clinical work and that in the pre-clinical teaching of pharmacology the therapeutic applications should be omitted except in so far as they are necessary to illustrate important principles. It is, however, desirable that the teaching of toxicology, which at present normally forms part of the course in forensic medicine, should take place during the second year of medical studies and be part of the course in pharmacology referred to above. At the final examination the student's knowledge of the physiological and therapeutical aspects of pharmacology including toxicology should be tested."

I think it is a fair comment on these recommendations that this Conference, if it did not openly discourage separate pharmacological laboratories, was at any rate lukewarm in its advocacy of them. It states that much of the practical pharmacology course might be carried out in a Department of Physiology. There would be little point or advantage in this if it left a residuum of practical pharmacology to be taught in a pharmacological laboratory. Does it not suggest rather a move towards the abolition of the separate pharmacological laboratory and its inclusion in the physiological department? The probability of this suggestion is enhanced by the positive recommendation of the Conference that a separate examination in pharmacology be discontinued and replaced by pharmacological questions in some part of the examination in physiology. The Conference could hardly have gone farther without actually stating that, from the point of view of medical teaching,

pharmacology could, without loss, be regarded as a mere appanage of physiology. I myself gave evidence before this Conference against this view and I take this opportunity of restating some of the arguments against it. It may at once be said that this is not a plea for a separate building for pharmacology; the housing together of physiology and pharmacology has even certain advantages. What matters is that pharmacology must have its own accommodation and direction and should be taught in accordance with its own outlook which is not identical with that of pure physiology. The proposal to include pharmacology as part of physiology is no novel idea. It is an experiment which has already been repeatedly made and with almost uniformly bad results, both for pharmacology and for the medical student.

Unless there is a definite academic career open to pharmacologists which in practice involves professorships and departments, men of ability cannot be expected to take the subject up. If a man is called upon to give, in a physiological department, "a short course of lectures and practical work" on pharmacology, when his interests and hopes of advancement lie in physiology rather than pharmacology, he can hardly be blamed for teaching pharmacology from the point of view of physiology and his students may know much about the actions of substances which have a conspicuous and easily demonstrable physiological action, however little their therapeutic value may be, but will probably know less about the remedies against diseases of worldwide importance like anthelmintics, trypanocides, &c., or even about the humbler but universally used agents to combat cough or diarrhœa. Moreover the literature on pharmacology is vast and increasing. No one man can hope to cover it all, still less cope simultaneously with the even greater literature on physiology. Also, unless pharmacology is to become a subject detached from therapeutics, the professed pharmacologist must, both in the interests of research and of teaching medical students, have a knowledge of the use of drugs in diseases and therefore of the diseases themselves. If pharmacology is so regarded, the subject is surely wide enough to absorb a man's whole energies, and a medical school cannot afford to dispense with a department and staff whose primary preoccupation it is to cover this territory.

The Conference from whose Report I have quoted recommends that: "In the preclinical teaching of pharmacology the therapeutic applications should be omitted except in so far as they are necessary to illustrate important principles." This exception might be variously interpreted but I am convinced, from long experience as a teacher and examiner, that the attempt to teach pharmacology to the medical student as a pure science and without continual reference to the therapeutic applications of drugs is doomed to failure. By the time he reaches pharmacology, the student has already studied half a dozen subjects as pure sciences and he is getting impatient to come closer to the application of those sciences to the practice of medicine. Naturally this must be done with some sense of proportion, but personally I have never found difficulty in explaining the therapeutic application of drugs to students even in the preclinical stage, and this has made all the difference in rousing the students' interest in the subject even as a pure science. Lastly, the Conference recommended that: "At the final examination the student's knowledge of the physiological and therapeutical aspects of pharmacology including toxicology should be tested", but no suggestion was made as to how, where, or by whom this test is to be conducted. It is difficult to avoid the conclusion that by this system of dealing with pharmacology there is a danger that the student's knowledge may be tested by a perfunctory examination in the preclinical stage and by a nondescript test in the final examination. The teaching of pharmacology as a basis for therapeutics, which is how it ought to be taught to the medical student, will be nobody's real business.

The Future of Pharmacology

The chief aims of medicine are the prevention and treatment of disease. The value placed upon chemical agents in the treatment of disease has had many ups and downs in the history of medicine, but at no time has this value been more fully accepted than at present. Therapeutics, based on pharmacology, is gradually being established upon a broader and sounder foundation, and the number and variety of remedies are increasing. The amount of research devoted to the discovery of new remedies is great and, apart from some unforeseen revolution in therapeutics, will increase. The investigation of new synthetic compounds is one of the most important functions of pharmacology, and for

this general pharmacology is needed, with the co-operation of synthetic chemistry and of bacteriology as well as of physiology.

The determination of the precise site and nature of the action of drugs and the explanation of the physical and chemical processes which underline pharmacological activity are main aims of pharmacology as a pure science. A fuller knowledge of these processes will, directly and indirectly, promote advance even in practical therapeutics. But academic pharmacology, if it encourages too exclusive a devotion to particular pharmacology and too early a specialization in it, may lose touch with practical therapeutics and fail to take an adequate share in the search for new remedies; in which case this search may be left to commercial laboratories which may, for work of this kind, possess facilities and resources greater than those of academic laboratories. It is important for British Medicine that medical schools should provide adequate facilities and support for general pharmacological research including chemotherapy, so that we should not fall behind other countries in this endeavour.

Knowledge of the application of pharmacology to therapeutics is essential for medical practice and medical schools must make adequate provision for imparting this knowledge. This cannot well be done by regarding pharmacology merely as a branch of physiology, for many of the most important uses of drugs bring pharmacology into as close relations with bacteriology as with physiology. The attempt to incorporate the teaching of pharmacology with that of physiology will almost certainly result in the subject being considered from too restricted a point of view and with insufficient relation to practical therapeutics.

The scope of pharmacology is sufficiently wide and its outlook sufficiently individualistic to warrant its being regarded, both for research and teaching, as an independent discipline. Unless it is given this status in medical schools and adequate provision made for it in the way of separate accommodation, staff, and support, it is unlikely that medical students will be properly taught the actions and uses of drugs or that pharmacological research, as subservient to therapeutics, will be sufficiently encouraged.

Section of Anæsthetics

President—H. N. WEBBER, B.Ch.

[*April* 4, 1941]

Anæsthesia in Chest Surgery, with Special Reference to Controlled Respiration and Cyclopropane

By M. D. NOSWORTHY, M.D.

ABSTRACT.—*Problems in chest surgery:* Cases with prolonged toxæmia or amyloid disease require an anæsthetic agent of low toxicity. When sputum or blood are present in the tracheobronchial tree the anæsthetic technique must prevent any spread to the unaffected parts. Inhalation anæsthesia should abolish reflex disturbances and excessive sputum be removed by suction. The technique should permit the use of a high oxygen atmosphere; controlled respiration with cyclopropane or ether fulfil these requirements. Open pneumothorax is present when a wound of the chest wall allows air to pass in and out of the pleural cavity. The lung on the affected side collapses and the mediastinum moves over and partly compresses the other lung.

The dangers of an open pneumothorax: (1) Paradoxical respiration—the lung on the affected side partially inflates on expiration and collapses on inspiration. Part of the air entering the good lung has been shuttled back from the lung on the affected side and is therefore vitiated. Full expansion of the sound lung is handicapped by the initial displacement of the mediastinum which increases on inspiration. The circulation becomes embarrassed.

(2) Vicious circle coughing. During a paroxysm of coughing dyspnœa will occur. This accentuates paradoxical respiration and starts a vicious circle. Death from asphyxia may result.

Special duties of the anæsthetist: (1) To carry out or supervise continuous circulatory resuscitation. During a thoracotomy a drip blood transfusion maintains normal blood-pressure and pulse-rate.

(2) To maintain efficient respiration.

Positive pressure anæsthesia: Risk of impacting secretions in smaller bronchi with subsequent atelectasis; eventual risk of CO_2 poisoning without premonitory signs.

Controlled respiration: (1) How it is produced. (2) Its uses in chest surgery.

Controlled respiration means that the anæsthetist, having abolished the active respiratory efforts of the patient, maintains an efficient tidal exchange by rhythmic squeezing of the breathing bag. This may be done mechanically by Crafoord's modification of Frenkner's spiropulsator or by hand.

Active respiration will cease (i) if the patient's CO_2 is lowered sufficiently by hyperventilation, (ii) if the patient's respiratory centre is depressed sufficiently by sedative and anæsthetic drugs, and (iii) by a combination of (i) and (ii) of less degree.

The author uses the second method, depressing the respiratory centre with omnopon-scopolamine, pentothal sodium, and then cyclopropane. *The CO_2 absorption method* is

essential for this technique, and this and controlled respiration should be mastered by the anæsthetist with a familiar agent and used at first only in uncomplicated cases.

The significance of cardiac arrhythmias occurring with cyclopropane is discussed.

The place of the other available anæsthetic agents is discussed particularly on the advisability of using local anæsthesia for the drainage of empyema or lung abscess.

Pharyngeal airway or endotracheal tube? Anæsthesia may be maintained with a pharyngeal airway in many cases but intubation must be used when tracheobronchial suction may be necessary and when there may be difficulty in maintaining an unobstructed airway.

A one-lung anæsthesia is ideal for pneumonectomy. This may be obtained by endotracheal anæsthesia after bronchial tamponage of the affected side (Crafoord, *v.* fig. 6*b*) or by an endobronchial intubation of the sound side (*v.* figs. 9*b* and 9*c*). Endobronchial placing of the breathing tube may be performed "blind". Before deciding on blind bronchial intubation, the anæsthetist must examine X-ray films for any abnormality deviating the trachea or bronchi. Though the right bronchus may be easily intubated blindly as a rule, there is the risk of occluding the orifice of the upper lobe bronchus (fig. 9*d*) when the patient will become cyanosed. If the tube bevel is facing its orifice the risk of occlusion will be decreased (fig. 9*c*).

Greater accuracy in placing the tube can be effected by inserting it under direct vision. Instruments for performing this manœuvre are described.

In lobectomy for bronchiectasis the anæsthetist must try to prevent the spread of infection to other parts. Ideally, the bronchus of the affected lobe should be plugged with ribbon gauze (Crafoord, *v.* fig. 6*c*) or a suction catheter with a baby balloon on it placed in the affected bronchus. In the presence of a large bronchopleural fistula controlled respiration cannot be established during operation. As the surgeon is rarely able to plug the fistula, if pneumonectomy is to be performed intubation for a one-lung anæsthesia is the best method. During other procedures it is essential to maintain quiet respiration.

In war casualties it is almost always possible, with the technique described, to leave the lung on the affected side fully expanded and thus frequently to restore normal respiratory physiology. Co-operation between surgeon and anæsthetist is essential.

RÉSUMÉ.—*Problèmes dans la chirurgie du thorax*: Dans les toxémies de longue durée et dans l'amyloïdose il est nécessaire d'employer un anesthésique peu toxique. S'il y a du sang ou du crachat dans l'arbre trachéobronchique il faut employer une méthode qui évite leur extension aux parties non affectées. L'anesthésie par inhalation doit abolir les troubles des réflexes, et l'excès de crachat doit être enlevé par l'aspiration. La technique doit permettre d'employer une atmosphère riche en oxygène. Ces conditions peuvent être satisfaites par la respiration contrôlée avec de l'éther ou du cyclopropane. Quand une plaie de la paroi thoracique permet à l'air d'entrer et de sortir de la cavité pleurale il existe un pneumothorax ouvert. Le poumon du côté affecté se dégonfle et le médiastin se déplace et comprime partiellement l'autre poumon.

Dangers du pneumothorax ouvert: (1) La respiration paradoxale: le poumon du côté affecté se remplit partiellement pendant l'expiration et se dégonfle pendant l'inspiration. Une partie de l'air qui entre dans le poumon sain revient du poumon affecté, et, par conséquent, est vicié. L'expansion complète du poumon sain est rendue difficile par le déplacement du médiastin, qui augmente pendant l'inspiration. La circulation devient gênée.

(2) La toux en cercle vicieux. L'accès de toux est accompagné de dyspnée, ce qui accentue la respiration paradoxale, et met en train un cercle vicieux. La mort par asphyxie peut en résulter.

Devoirs spéciaux de l'anesthésiste: (1) Surveillance ou exécution de mesures continues pour stimuler la circulation. Une transfusion de sang goutte à goutte pendant une thoracotomie maintient la pression sanguine et le pouls au niveau normal.

(2) Maintenance d'une respiration effective.

Anesthésie à pression positive: Risque de l'impaction des sécrétions dans les petites bronches, produisant l'atélectasie du poumon. Risque éventuel d'empoisonnement par le CO_2 sans signes prémonitoires.

Respiration contrôlée: (1) Technique de sa production. (2) Son emploi dans la chirurgie thoracique.

Dans la respiration contrôlée, le chirurgien, après avoir aboli l'effort respiratoire du malade, maintient un échange d'air effectif en comprimant rythmiquement le sac respiratoire. Ceci peut être exécuté mécaniquement par le spiropulsateur de Frenkner modifié par Crafoord, ou à la main.

La respiration active cessera (i) si le taux de CO_2 est suffisamment diminué par l'hyperventilation, (ii) si le centre respiratoire est suffisamment déprimé par des médicaments sédatifs ou anesthésiques, et (iii) par la combinaison de degrés plus faibles de ces deux conditions.

L'auteur emploie la seconde méthode, déprimant le centre respiratoire avec l'omnopon-scopolamine et le pentothal sodium, suivis de cyclopropane. Dans cette méthode la *technique avec absorption de* CO_2 est essentielle, et l'anesthésiste doit l'apprendre à fond avec un anesthésique qu'il connaît bien, et l'employer, pour commencer, seulement dans les cas sans complications.

L'auteur discute l'importance des arythmies cardiaques pendant l'anesthésie au cyclopropane.

L'emploi des autres anesthésiques disponibles est discutée, et surtout l'utilité de l'anesthésie locale pour le drainage des empyèmes ou des abcès pulmonaires.

Passage de l'air par le pharynx ou par un tube trachéal? Dans beaucoup de cas l'anesthésie peut être maintenue avec un passage à air pharyngien, mais l'intubation trachéale doit être faite s'il est possible que l'aspiration trachéobronchique devienne nécessaire, ou qu'il devienne difficile de maintenir un passage sans obstruction.

L'anesthésie à un poumon est la méthode idéale pour la pneumonectomie. Elle peut être produite par l'anesthésie endotrachéale après tamponnement des bronches du poumon opposé (Crafoord, v. fig. 6*b*) ou par l'intubation endobronchique du côté sain (v. fig. 9*b* et 9*c*). L'introduction du tube respiratoire endobronchique peut être exécutée "à l'aveugle". Avant de se décider à introduire le tube "à l'aveugle", l'anesthésiste doit examiner les radiographies des poumons pour déceler toute anomalie produisant une déviation de la trachée ou des bronches. Quoiqu'il soit facile, dans la plupart des cas, de passer un tube "à l'aveugle" dans la bronche droite, il y a un risque de bloquer l'orifice de la bronche du lobe supérieur gauche (fig. 9*d*), et le malade devient cyanosé. Si le biseau du tube est en face de l'orifice le risque d'occlusion est diminué (fig. 9*c*).

Le tube peut être introduit avec plus d'exactitude sous vision directe. L'auteur décrit les instruments employés pour cette manoeuvre.

Dans les lobectomies pour bronchiectasie, l'anesthésiste doit essayer d'empêcher l'extension de l'infection. Il est idéal de tamponner la bronche du lobe affecté avec de la gaze en ruban (Crafoord, v. fig. 6*c*) ou par un cathéter à aspiration muni d'un petit ballon. La respiration contrôlée ne peut pas être instituée pendant l'opération dans les cas où il existe une grande fistule broncho-pleurale. Comme il est rare que le chirurgien puisse boucher la fistule, l'intubation pour une anesthésie à un poumon est la meilleure méthode si une pneumonectomie doit être faite. Dans d'autres interventions il est essentiel de maintenir une respiration tranquille.

Chez les blessés de guerre il est presque toujours possible, avec la technique décrite ici, de laisser le poumon du côté affecté entièrement dilaté, et, par ce moyen, de restaurer la respiration physiologique dans beaucoup de cas. La co-opération entre l'anesthésiste et le chirurgien est essentielle.

RESUMEN.—*Problemas de cirugía torácica*: Los casos que presentan toxemia prolongada o enfermedad amiloidea necesitan un agente anestésico de baja toxicidad. Cuando el esputo o la sangre encóntrase en el arbol traqueobronquial la técnica anestésica tiene que prevenir su extensión a las regiones sanas. La anestesia por inhalación debiera abolir accidentes reflejos y el esputo excesivo llevarse por aspiración. La técnica debiera permitir el uso de una atmósfera con elevada proporción de oxígeno. Realiza estos requisitos la respiración controlada con ciclopropane o éter. El neumotórax abierto está presente cuando una herida de la pared torácica permite el ingreso o salida de aire en la cavidad pleural. El pulmón del lado afectado sufre colapso y el mediastino se desvía y comprime en parte el otro pulmón.

Los peligros de un neumotórax abierto: (1) Respiración paradojal—el pulmón del lado afectado se infla parcialmente al espirar y sufre colapso al inspirar. Una parte del aire entrando en el pulmón indemne ha sido expulsada del pulmón del lado afectado y

está por consecuencia viciada. Molesta a la completa distensión del pulmón sano la desviación inicial del mediastino, la cual se exagera al inspirar. La circulación se perturba.

(2) La tos en círculo vicioso. Durante un paroxismo de toser occure la dispnea. Ésta acentúa la respiración paradojal e inaugura un círculo vicioso. Puede terminar en el muerte por asfixia.

Tareas particulares del anestesiador: (1) El ejecutar o vigilar resucitación circulatoria continua. Pendente una toracotomía una trasfusión sanguínea a gotas mantiene la tensión y el número de pulsaciones normales.

(2) El mantener una respiración eficiente.

Anestesia por presión positiva: riesgo de empaquetar secreciones en los bronquios menores, seguidas de atelectasia; riesgo último de asfixia por CO_2 sin advertencia alguna.

Respiración controlada: (1) Como se produce. (2) Sus aplicaciones a la cirugía torácica.

La respiración controlada significa que, suprimidos los esfuerzos respiratorios activos del paciente, el anestesiador sostiene un cambio periódico eficaz por compresión rítmica de la bolsa. Este se hace o por mano o mecánicamente, utilizando la modificación que efectuó Crafoord al spiropulsator de Frenkner.

Cesará la respiración activa (i) si el CO_2 del paciente se rebaja bastante por hiperventilación, (ii) si el centro respiratorio del paciente se deprime bastante por los medicamentos calmantes y anestésicos, y (iii) por una combinación de (i) y (ii).

El autor practica el segundo método, deprimiendo el centro con omnopon-scopolamine, pentotal sódico, y después con ciclopropane. *El método de absorción de CO_2* es esencial para esta técnica, y el anestesiador debe le dominar así como la respiración controlada, usando agentes conocidos y al principio sólo en casos sin complicación.

Se habló de la significación de arritmias cardíacas occuriendo con el ciclopropane.

Tratóse del *empleo de los otros anestésicos disponibles*, y se consideraron sobre todo las ventajas de usar anestesia local para el drenaje de empiema o absceso pulmonar.

Conducto faríngeo o tubo endotraqueal? La anestesia se mantiene a menudo por vía faríngea, pero ha de emplearse la intubación siempre que sea necesaria la succión traqueobronquial y que haya dificultad en guardar un libre conducto de aire.

Anestesia de un solo pulmón es ideal en neumonectomía. Se puede obtener por anestesia endotraqueal después de taponamiento bronquial del lado afectado (Crafoord, v. fig. 6*b*), o por intubación endobronquial del lado sano (v. fig. 9*b* y 9*c*). El tubo endobronquial puede colocarse "a ciegas". Antes de resolverse para la intubación bronquial ciega el anestesiador debe examinar radiogramas por desviación anormal de la tráquea o los bronquios. Aunque por lo general la intubación ciega del bronquio derecho se ejecute fácilmente, se arriesga de ocluir el orificio del bronquio del lóbulo superior (fig. 9*d*) y de que el paciente se vuelva cianosado. El riesgo de oclusión decrece si el bisel del tubo hace frente a su orificio (fig. 9*c*).

Se insinúa más exactamente el tubo bajo visión directa. Los instrumentos necesarios se describen.

En lobectomía para bronquiectasia debe esmerarse el anestesiador para evitar la extensión de la infección a otras regiones. Lo mejor es taponar el bronquio del lóbulo afectado con cinta de gasa (Crafoord, v. fig. 6*c*) o colocar un catéter de succión proveído de balón pequeño al bronquio enfermo. En presencia de una gran fístula broncopleural no puede establecerse pendente intervención la respiración controlada. El cirujano pudiendo taponar rara vez la fístula en casos de neumonectomía la anestesia por intubación de un solo pulmón constituye el mejor método. Durante otros procedimientos el mantener una respiración tranquila es esencial.

En los heridos de guerra la técnica descrita dejará casi siempre enteramente dilatado el pulmón del lado afectado y restituirá así a menudo la respiración normal fisiológica. Es indispensable la cooperación entre cirujano y anestesiador.

Resumo.—*Problemas da cirurgia do peito*: Os casos com toxemia prolongada ou doença amiloide exigem um agente anestetico de baixa toxicidade. Quando aparece expectoração ou sangue na arvore traqueiobronquica a tecnica anestetica deve evitar qualquer extenção para as partes não afetadas. A anestesia por inalação deve abolir disturbios reflexos e a expectoração demasiada deve ser removida por sucção. O tecnico deve permitir o uso de uma atemosfera fortemente oxigenada; e o controle da respiração com cyclopropane ou com éter satisfaz estes requesitos. O pneumotorax aberto aparece quando uma ferida da parede toraxica deixa passar o ar para dentro e para fóra da cavidade pleural.

O pulmão no lado afetado esvasia-se e o mediastinio move'-se e comprime parcialmente o outro pulmão.

Perigos de um pneumotorax aberto: (1) Respiração paradoxal—o pulmão no lado afetado enche'-se na expiração e esvasia-se na inspiração. Parte do ar que entra no pulmão bom foi rechaçado do pulmão no lado afetado e extá portanto viciado. A expanção ampla do pulmão saudavel é dificultada pelo deslocamento inicial do mediastinio que aumenta com a inspiração. A circulação torna-se dificultosa.

(2) Tosse em circulo vicioso. Durante um paroxismo de tosse aparece dispeneia. Isto acentua a respiração paradoxica e dá origem ao circulo vicioso. Disto pode resultar a morte por asfixia.

Deveres especiaes do anestesiador: (1) Fazer ou superintender a revivescencia circulatoria continua. Durante uma toracotomia uma transfusãodo sangue por gotas mantem pressão normal do sangue e o ritmo do pulso.

(2) Para manter respiração eficaz.

Anestesia por pressão positiva: risco de forçar secreções nos bronquiolos mais pequenos com a subsequente atelectases; risco consequente de envenenamento por CO_2 sem sinaes premonitorios.

Respiração controlada: (1) Como se procede. (2) O seu uso na cirurgia do peito.

Respiração controlada quer dizer que o anestesiador, tendo abolido os esforços ativos da respiração do doente, mantem uma eficaz permuta, em ambos os sentidos, com a compressão ritimica do saco respiratorio. Isto pode fazer-se mecanicamente pela modificação Crafoord do espiropulsador de Frenkner, or com a mão.

A respiração activa pára se (1) o CO_2 do doente for baixado suficientemente pela hiperventilação, (11) se o centro respiratorio do doente estiver deprimido suficientemente pelos sedativos e medicamentos anesteticos, e (222) pela combinação de (1) e (2) de uma forma menos intensa.

O autor emprega o segundo metodo, deprimindo o centro respiratorio com omopon-escopolamina, pentotal de sodio, e depois cyclopropanio. *O metodo de absorção de* CO_2 é essencial para esta execução, e isto e a respiração controlada devem estar sob o dominio do anestesiador com um agente intimo e empregado sómente, ao principio, em casos sem complicações.

A importancia das arritmias cardiacas resultantes do cyclopropane é materia de discussão.

O logar ocupado pelos outros agentes anesteticos dispeniveis foi discutido particularmente sobre a vantagem de usar a anestesia local para drenar o empiema ou o abcesso do pulmão.

Passagem aerea da faringe ou tubo endotraqueal? Pode manter-se a anestesia pela passagem faringea em muitos casos, mas a intubação deve ser usada quando possa ser necessaria a succão traqueio-bronquica e quando possa haver dificuldade em manter a passagem desobstruida.

A anestesia de um so pulmão é ideal para a pneumonectomia. Isto pode conseguir-se pela anestesia endotraqueal depois da colocação de tampões no lado afetado (Crafoord, v. fig. 6*b*), ou pel intubação endobronquial do lado são (v. fig. 9*b* e 9*c*). A colocação endobronquial do tubo respirador pode ser feita " ás cegas ". Antes de se decidir fazer a intubacão bronquial ás cegas o anestesiador deve examinar as peliculas dos raios X para ver se encontra qualquer desvio anormal da traqueia ou dos bronquios. Embora o bronquio direito possa ser facilmente intubado ás cegas, em geral, ha porem o perigo de tapar o orificio do lobulo superior do bronquio (fig. 9*d*) quando o doente fica cianosado. Se o rebordo do tubo enfrenta o orificio o risco de oclusão é menor (fig. 9*c*).

A colocação do tubo pode fazer-se com muito maior certeza, quando se faz á vista direta. Descrevem-se os instrumentos para fazer este manejo.

Na lobectomia para a bronquietasia o anestesiador deve esforçar-se em evitar o desenvolvimento da infeção para as outras partes. Idealmente, o bronquio do lobolo afetado deve ser tapado com uma fita de gaze (Crafoord, v. fig. 6*c*) ou um catetér de aspiração com um pequeno balãosinho colocado no bronquio afetado. Em presença de uma grande fistula bronquio-pleural não se pode obter respiração controlada durante a operação. Como o cirurgião raras veses pode obturar a fistula se se tiver de fazer a pneumonectomia, o melhor metodo é a intubação para a anestesia de um pulmão. Durante outros processos é essencial manter uma respiração tranquila.

Nas casualidades da guerra é quasi sempre possivel com a tecnica descrita deixar o pulmão do lado afetado amplamente expandido e assim restaurar frequentemente a fisiologia respiratoria normal. A cooperação do anestesiador e do circurgião é essencial.

FIVE years ago Magill (1936) stated that "the whole position (of anæsthesia in thoracic surgery) will bear revision and some recapitulation not only now but again at no very distant date". When I was asked to read this paper I was loath to do so because too much of the subject still remains a mystery to me. I shall, therefore, first present the problems as I see them and then explain how I tackle them, giving my reasons for the choice of various techniques for different types of cases.

The ordinary civilian sick seldom require emergency chest operations, and their reserve will therefore have been built up as far as possible before they come to surgery. Many of these, however, are more or less chronic invalids. They may have had prolonged toxæmia and be suffering from amyloid disease. The least toxic agent which is capable of producing satisfactory anæsthesia is therefore indicated. I hope to show that nitrous oxide does not fulfil this requirement in chest surgery.

When sputum, or blood and sputum are present in the tracheobronchial tree, the anæsthetic technique must be such that any spread to the unaffected lung zones is prevented. A patient with bronchiectasis may produce no sputum—even after postural drainage—before operation, and yet bring up large quantities as soon as an inhalation anæsthetic is started. The affected lobe may be like a sponge and only let loose its contents in gushes each time the surgeon handles it. Churchill, Professor of Surgery at Harvard, believes that any coughing or straining during anæsthesia is liable to spread infection to normal lung tissue. I am convinced that inhalation anæsthesia should be deep enough to abolish all reflex disturbance. One has only to notice the difference between the bronchograms of patients who have and those who have not coughed after the introduction of the lipiodol to realize how easily coughing or straining may disseminate the infection. When sputum is present in any quantity, therefore, it should be shut off in the affected zone or else removed by suction.

In chest surgery the reflexes should return as soon as possible after the operation so that any secretion can be actively coughed up. The protracted recovery period rules out the use of avertin or paraldehyde except for children. The giving of pentothal sodium throughout long chest operations has the same disadvantage.

Chest patients commonly have a low vital capacity. The lateral position on the operating table handicaps them still further and may cause dyspnœa. The anæsthetic technique should, therefore, make full use of what alveolar membrane there is available for gaseous interchange, and should permit the use of a high oxygen atmosphere. Controlled respiration with cyclopropane or ether fulfils these requirements.

People who have been bombed are usually frightened, and if they have coughed up blood think they are going to die. They must be reassured and calmed. Patients with chest injuries not requiring immediate surgery will be prepared for operation in the usual way. Casualties requiring immediate operation may have had a meal only a short time before being injured. Guedel told me that he induces anæsthesia with evipan sodium when the patient has a full stomach. I have very frequently given pentothal sodium but consider that the chief thing is to make a fast, smooth induction so that the patient is carried rapidly below the level of the vomiting reflex.

It is obviously useless to carry out heroic intrathoracic surgery on war casualties who have not responded to resuscitative measures. Many of the patients selected for operation, however, are suffering from various degrees of shock and oxygen want; and in spite of warmth, morphine, oxygen therapy, and blood transfusion their condition may improve but little. It has been my experience that these patients stand up surprisingly well to quite lengthy procedures provided normal physiological function is finally restored. Thus, when disturbance of his cardio-respiratory physiology due to a chest full of blood-clot or an open pneumothorax, or hæmorrhage from an intercostal vessel is the primary factor which is incapacitating the patient, it is better not to wait too long in the hope of improvement in his condition, but to operate and put things right while treatment for shock is continued.

Even when all blood loss is made good, loss of body heat is a deciding factor in how much can be done inside the chest. Loss of heat is considerable when the chest wall is widely opened especially if there is a large, raw surface exposed. The time factor will obviously vary with the physique of the individual patient.

Open pneumothorax presents a complex problem and a number of factors must be taken into consideration. How many of these factors will be involved, and which will play the most important role, will vary with the nature of the case. Its dangers must be viewed not only from the respiratory but also from the circulatory standpoint.

An open pneumothorax is present when a wound of the chest wall allows air to pass in and out of the pleural cavity. The lung on the affected side collapses, and the mediastinum moves over and to some extent compresses the other lung. When the capacity of the thorax increases there is now, on inspiration, a competition between the air entering the pleural cavity through the opening in the chest wall and that entering the lung through the glottis. If the opening in the chest wall is small, partial expansion of the lung takes place and respiration need not be greatly embarrassed. The size of the patient's vital capacity will influence the effects of an open pneumothorax. With a widely opened chest wall the relative pressures are such that no air enters the affected lung during the inspiratory phase. On the contrary, the lung on the affected side collapses still further on inspiration since air is drawn from it over to the sound lung. When the capacity of the thorax decreases during expiration the lung on the sound side discharges its contents partly up the trachea and partly into the collapsed lung. This to-and-fro movement of air from one lung to the other makes the movements of the lung on the affected side paradoxical since it expands with expiration and collapses with inspiration (fig. 1).

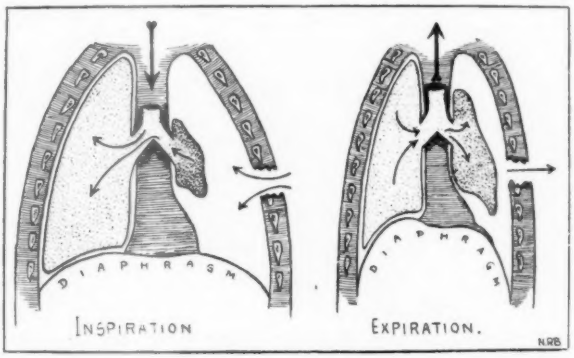


FIG. 1.—Paradoxical respiratory movements resulting from an open pneumothorax.

Paradoxical respiration makes the patient incapable of making efficient use of even one lung since part of the air which enters it is that which has been shuttled back from the lung on the affected side and is therefore vitiated. In addition, full expansion of the sound lung is handicapped by the initial displacement of the mediastinum and expansion is still further curtailed by an increase in this displacement on inspiration.

Loss of the normal negative pressure in the chest adversely affects the return of blood to the heart. The initial displacement and to-and-fro movement of the mediastinum interferes with the continuous flow in the great veins by periodically causing partial obstruction to the superior and inferior vena cava. Consequently the heart does not fill so well and it is not surprising that open pneumothorax and paradoxical respiration embarrass the circulation.

Although a patient may be bearing up quite well in spite of an open pneumothorax he may very quickly be reduced to a moribund condition by a sudden fit of coughing. This may be initiated, whenever there is active disease in the lung such as an abscess, pneumonia, or bronchiectasis, by secretions moving on to a sensitive piece of mucous membrane. During the paroxysm of coughing the patient is incapable of breathing efficiently and he is likely, therefore, to become dyspnœic. Dyspnœa accentuates all the ill-effects of paradoxical respiration and starts a vicious circle which may prove fatal. The phrase "vicious circle coughing" might well be coined to describe this sequence of events.

Though we have all seen patients doing well under local or spinal anæsthesia in spite of an open pneumothorax, we have also seen—though we may not all have appreciated it

—a patient or two dying as a result of paradoxical movements, and death from asphyxia is not a pretty sight. It will be well, therefore, to understand why one patient will tolerate an open pneumothorax better than another.

When the mediastinum is rigid it will not move across and press on the sound lung, nor will it move to-and-fro with respiration and embarrass the circulation. The presence of pleural adhesions on the affected side will hold the lung out and prevent it from collapsing, and on respiration it will move with the chest wall. So long as a patient breathes quietly and still satisfies his respiratory requirements he may not be embarrassed by a mild degree of paradoxical movement.

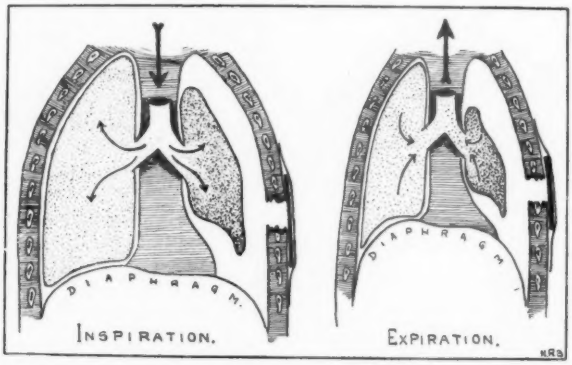


FIG. 2.—Respiratory movements no longer paradoxical on closure of an open pneumothorax.

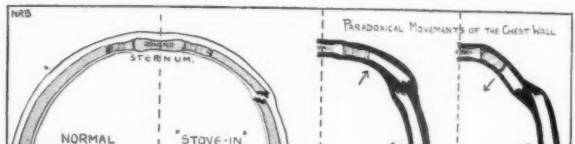


FIG. 3.—Paradoxical respiration due to a " stove-in " chest.

(FIGS. 1, 2 and 3 are reproduced by courtesy of Mr. N. R. Barrett and of the *Nursing Times*.)

" Sucking " wounds (figs. 1 and 2) and " stove in " chest (fig. 3) are associated with paradoxical respiration, to control which the affected area should be covered with vaseline gauze and immobilized with strapping as soon as possible. Thoracoplasty will give rise to paradoxical movements which, under local anæsthesia, the surgeon must himself control by pressing a hand or a pack over the affected part. Paradoxical respiration was a common cause of post-operative death in the past when too many ribs were removed at one session. In any thoracotomy the anæsthetist must be prepared to counteract paradoxical respiration the effects of which might otherwise eventually prove lethal. With

efficient anæsthesia the need for applying traction to the lung and drawing it into the wound in order to offset the effects of open pneumothorax is a thing of the past.

Special Duties of the Anæsthetist

Firstly, the anæsthetist must be prepared to carry out or supervise continuous circulatory resuscitation, and secondly, he must make sure that efficient respiration is taking place. These two duties apply with equal force to a major procedure anywhere in the body.

During a major operation the anæsthetist should not wait for the signs of circulatory depression but, if he judges that the patient's powers of compensation are being taxed, he should institute resuscitative measures without waiting for changes in blood-pressure or pulse-rate to occur.

Although lobectomy and pneumonectomy are frequently performed without intravenous therapy there is no doubt that those who receive blood during a thoracotomy leave the theatre in a more normal condition. We now set up a drip blood transfusion before beginning a thoracotomy. Having it already set up gives one a feeling of confidence since there need be no delay in restoring blood loss should brisk hæmorrhage occur. The drip is left running slowly and the rate speeded up if vascular adhesions have to be divided to expose the lung. The speed of the transfusion and the quantity of blood given should be decided by the anæsthetist. The surgeon is too occupied with his own work and is not in a position to know what the patient requires. My aim is to replace blood as it is lost and to maintain a normal blood-pressure and pulse-rate. In one very difficult and hæmorrhagic pneumonectomy as much as 4 pints of blood were given during the three and a quarter hours taken to complete the operation, at the end of which the patient had a blood-pressure of 120/70 and a pulse-rate of 90.

The maintenance of efficient respiration is of the first importance during all operations. But in chest surgery it takes on special significance since without the elimination of paradoxical movements respiration cannot be called efficient.

It has been commonly stated in the past that positive pressure should be used when necessary to control "mediastinal flap". Crafoord of Stockholm (1938) considers that positive pressure anæsthesia does not provide efficient respiration since the lungs are not effectively emptied. He produces experimental evidence in the dog to show that under positive pressure anæsthesia the blood CO_2 steadily rises, and unless a change is made to rhythmical ventilation the animal will eventually die of CO_2 poisoning. Crafoord maintains that when a slow but steady rise in CO_2 occurs there may be no outward and visible signs to warn the anæsthetist that the patient is reaching breaking point before the heart dilates and the patient is gone. Beecher of Harvard (1940) on the other hand advocates positive pressure anæsthesia and has not found a rise in CO_2 in a small series of blood estimations. He disapproves of rhythmical ventilation (or controlled respiration) on the ground that with the abolition of active breathing the anæsthetist loses his chief guide to the depth of narcosis. I was under the impression that the drawbacks to positive pressure anæsthesia were well established—for instance, the impaction of secretions in the smaller bronchi with subsequent peripheral atelectasis—and that it was only tolerated as a lesser evil than mediastinal flap for the want of something better. Having no personal experimental evidence I cannot be dogmatic. It did occur to me, however, when reading Beecher's paper that—since so many of his patients had been subjected to lobectomy—a possible explanation of his normal blood CO_2 findings might have been the presence of pleural adhesions which would enable him to get along with little, or only intermittent positive pressure. Beecher also questions the advisability of producing an alkalosis in chest patients by hyperventilation. Waters and Seevers of Madison have found no ill-effects after prolonged hyperventilation in the dog, and by the method of controlled respiration which I employ there is no reason for the patient's CO_2 to be abnormally low. Practically all our war casualties have had a freely mobile mediastinum without previous pleural adhesions, and there can be no question that controlled respiration has not only abolished the dangers of an open pneumothorax but has also provided efficient respiration. On controlled respiration our patients' condition has been such that I personally should be loath to revert to any other method. Controlled respiration is not difficult but, like any other technique, it should be learnt during simple operations.

Controlled Respiration

Guedel, I believe, was the first man to make use of controlled respiration, and its advantages in chest surgery are as follows: The dangers of an open pneumothorax are completely abolished. Both pleural cavities can be opened simultaneously without any upset. The patient's existing vital capacity is used to the full, and adequate oxygenation and efficient removal of CO_2 are ensured. If the surgeon has to perform a difficult suture deep in the chest the lungs can be left completely at rest for a minute or so at a time. The administration of the anæsthetic can be interrupted to permit aspiration of the tracheobronchial tree without the return of paradoxical respiration as occurs on the interruption of a positive pressure anæsthesia.

The term controlled respiration signifies that the anæsthetist, having abolished the active respiratory efforts of the patient, maintains an efficient tidal exchange by rhythmic squeezing of the breathing bag. This may be performed mechanically by Crafoord's modification of Frenkner's spiropulsator, or more simply and just as effectively—if the anæsthetist appreciates what he is doing—by hand. Although the technique is on similar lines to that used for artificial respiration and resuscitation of an overdosed patient, the essential difference is that, in spite of the apnœa, one is frequently adding more of the anæsthetic agent instead of striving to get rid of it. Many will say that they prefer to have their patients breathing but I maintain that their patients' breathing is often not so efficient as my controlled respiration. No one who is familiar with controlled respiration will for choice use anything else inside the chest. During other operations surgeons may not know whether controlled respiration is being used or not, but inside the chest they recognize the difference at once. For chest surgery I always use the CO_2 absorption method which lends itself very readily to this technique.

Active respiration may be abolished in two ways or by a combination of the two. Firstly, the patient's CO_2 may be lowered until it no longer is in sufficient concentration to stimulate the respiratory centre. Secondly, the patient's respiratory centre may be depressed by sedative drugs and anæsthetic agents until it no longer responds to the *normal* concentration of CO_2—although if the CO_2 was not kept down to normal, shallow jerky inefficient respiration might be maintained at this depth by the CO_2 accumulation which this type of breathing entails. Finally, active respiration will also cease when the respiratory centre is less depressed provided this is associated with a slightly subnormal CO_2 (*see* Guedel's stimulus and threshold board (Nosworthy, 1939)). After respiration has been abolished by one of these methods the CO_2 reaccumulates or banks up in the ensuing apnœa, and would normally reactivate the respiratory centre in, say, half a minute. Before this, however, an artificial inspiration is brought about by the anæsthetist squeezing the breathing bag, and the passive expiration, which naturally follows on releasing the bag, lowers the CO_2 once more when it comes in contact with the soda-lime. Carrying on in this way one can keep the breathing in abeyance for as long as one chooses. There are two conditions which would obviously prevent the normal resumption of active breathing. Firstly, before sufficient reaccumulation or banking up of CO_2 could take place some patients might have used up so much of their available oxygen that respiration would not be spontaneously resumed. Secondly, if the apnœa is very deep the respiratory centre will be out of range of any CO_2 stimulation. In such circumstances one simply carries on respiration and makes the necessary adjustments. Provided one keeps constantly in mind how high or how low is the patient's CO_2 and how depressed is the respiratory centre, and adjusts them as circumstances demand, I can see no danger in the production or the maintenance of controlled respiration, and no difficulty in the restoration of normal breathing. Criticism of the technique reflects rather on the capabilities of the anæsthetist, and, in my opinion, it is unjustifiable to condemn a technique which has manifest advantages just because the administrator is unqualified to use it.

I personally never produce controlled respiration by the first method which I have described. To lower the CO_2 sufficiently to produce apnœa would require such hyperventilation that I consider pulmonary damage might result, especially when the lungs have been contused or perforated by missiles of war. I prefer to knock out the respiratory centre by depressant drugs during induction and then as the operation proceeds I can —if the nature of the surgery permits—lighten the depth of anæsthesia and still maintain controlled respiration, perhaps by keeping the CO_2 slightly subnormal. I will describe how this is done when I deal with cyclopropane which I have used for the vast majority of cases.

THE CO_2 ABSORPTION METHOD

The anæsthetist will obviously get into trouble if he embarks on controlled respiration before he has a full understanding of CO_2 absorption itself. For the same reason he

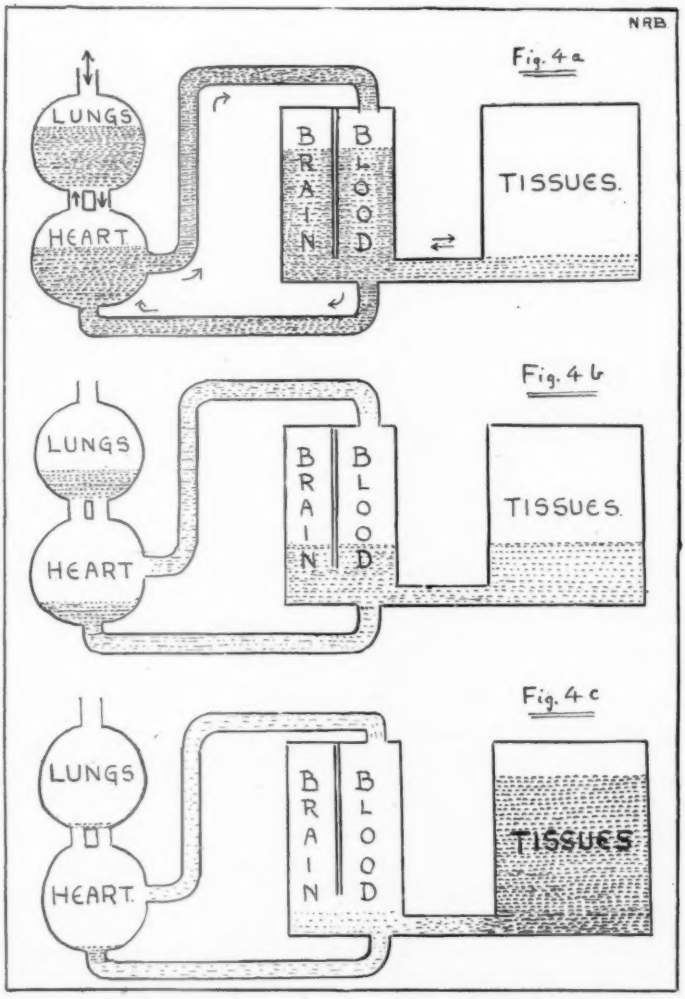


FIG. 4*a*, *b*, *c*.—The relative anæsthetic concentrations in the blood, the brain and the tissues during different phases of anæsthesia (*see* text).

will do better to master the CO_2 absorption principle with agents like ether and nitrous oxide with which he is already familiar, rather than to attempt the use of CO_2 absorption for the first time with a new agent like cyclopropane. A new technique with an unfamiliar method will land the anæsthetist in difficulties. I need not stress what is likely to happen

if the anæsthetist attempts to use a new technique, a new method, and a new agent all at the same time. My point is illustrated by a recent statement that the CO_2 absorption method is no good in chest surgery since it does not keep the CO_2 down. Of course, when a patient is breathing so inefficiently that he is merely shifting his dead space air up and down it is obvious that neither the absorption nor any other method will prevent him from having a high alveolar CO_2. An efficient tidal exchange must be maintained in every anæsthesia. There is a recent article by Adriani and Rovenstine of New York (1941) on the efficiency of CO_2 absorbers. They show that the best absorption results are obtained by having two canisters and using them alternately every hour. During chest surgery an efficient tidal exchange can often, in my opinion, only be obtained by controlled respiration.

For CO_2 absorption I use Waters's "to-and-fro" system in preference to "the circuit". When anæsthesia is started with the soda-lime canister "in" it is more difficult to make a smooth induction, and it certainly takes a much longer time to produce deep anæsthesia. I usually keep the canister "out" for a minute or two at the start and the deeper breathing from the CO_2 accumulation helps to make induction smooth and rapid. It must be borne in mind, however, that as soon as the soda-lime canister is inserted the CO_2 will quickly fall to normal or below normal, which may influence the anæsthesia in two respects. Firstly, the breathing will become shallower and may even cease for a time. Secondly, with the CO_2 now at the normal or subnormal level the larynx may not tolerate the same strength of ether vapour, and consequently, if this agent is being used, its concentration may have to be reduced after insertion of the canister. Both these changes will diminish the quantity of anæsthetic which is being absorbed into the bloodstream. Loss of anæsthetic from the brain to the tissues in an attempt to produce anæsthetic equilibrium throughout the body may exceed the quantity which is now being absorbed from the lungs, and the depth of anæsthesia will therefore lighten (figs. 4*a*→4*b*). So long as the anæsthetist appreciates these facts he will not have difficulty in coping with them.

Now, the depth of anæsthesia depends upon the brain saturation but the tissue saturation lags behind this, and it may take half an hour or more before the whole body is in anæsthetic equilibrium (fig. 4*b*). Therefore, although the required depth of anæsthesia has been attained, a little more anæsthetic must be constantly added for a time to make good that which spreads to the tissues—in spite of the entirely closed system. The quicker the induction the greater the difference between the brain and the tissue saturation (fig. 4*a*) and consequently the longer the time before the introduction of additional anæsthetic can be discontinued and the basal oxygen flow left running alone. It is important to recognize this when using controlled respiration.

Now we must consider the different anæsthetic agents and their uses in chest surgery.

LOCAL ANÆSTHESIA

This type of anæsthesia is commonly used for the following procedures:

(1) *Phrenic avulsion or crush.*

(2) *Bronchoscopy.*

(3) *The introduction of endotracheal tubes* in patients with copious sputum before the induction of general anæsthesia.

(4) *Drainage of empyema.*—I have given general anæsthesia for this to many war casualties. The danger lies in the risk that the patient may rupture the empyema into his bronchial tree and drown himself. I have had one patient who coughed and coughed during induction and evacuated the whole of his empyema in this way. Fortunately he had no sequelæ, but the case illustrates the danger and stresses the importance of a smooth induction if general anæsthesia has to be used because of sepsis in the chest wall. It is much safer, therefore, to use local anæsthesia; otherwise sooner or later a fatality will result. Although the presence of a bronchopleural fistula may not be suspected its presence may become obvious after making an opening in the pleura by the production of sputum. For this reason an empyema should be drained with the patient sitting up across the table or, if he is too ill to be placed in this position, the table should be arranged so that he is supported in the lateral position with his body almost upright.

(5) *Drainage of lung abscess* for the same reason as empyema.

(6) *The removal of hydatid cyst.*—If the pleura is free, a hydatid cyst should be treated by a two-stage operation like a lung abscess. If a one-stage operation is performed under

general—or local—anæsthesia two troubles may arise. Firstly, blood may enter the bronchial tree necessitating suction with the risk of possible spread. Secondly, such a large bronchopleural fistula may result that it will be impossible to keep the lung expanded with the subsequent risk of a total empyema, surgical emphysema, &c.

(7) *Thoracoplasty.*—Surgical opinion is swinging towards local anæsthesia plus, if necessary, obstetrical chloroform. Recently I have used on several occasions with success omnopon-scopolamine and pentothal followed by cyclopropane with controlled respiration.

(8) *For blocking the nerves at the hilum of the lung during dissection pneumonectomy.*—This practice prevents much reflex disturbance which I personally have not been able to control by injections of atropine. A long-acting drug should be used for it may be two and a half hours before the surgeon reaches the stage of sewing up the bronchus. When no local injection is used the inhalation anæsthesia must be more profound and when the effect of the local injection has worn off too soon pulse and blood-pressure changes are apt to occur—for instance, I have seen the blood-pressure become unrecordable or show only a very small pulse pressure during the bronchial closure itself, and then return to its previous readings. *Adrenaline should not be added to the local anæsthetic when cyclopropane is being used.* The one and only ventricular tachycardia which I have observed in chest surgery under this agent occurred after such an injection although it soon disappeared without apparent harm to the patient.

SPINAL ANÆSTHESIA

With unilateral spinal blocks I have had little success in chest surgery; but I have produced a sufficiently high spinal block with a modification of Etherington Wilson's technique to allow the performance of an upper stage thoracoplasty. However, the margin of safety is small and other methods are indicated.

Fit young adults with bronchiectasis and sputum often stand lobectomy very well under spinal anæsthesia. The cough so vital for getting rid of sputum is sometimes, however, ineffective. Then the patient may become dyspnœic and deteriorate rapidly. It is not uncommon to see the surgeon, after he has freed the lobe, at work beyond the vertebral column which means that ventilation is often inefficient under spinal anæsthesia.

I like my anæsthetic technique to be such that I have the whole situation under control. I do not feel that I am in a position to cope with any emergency when chest surgery is performed under spinal anæsthesia.

RECTAL ANÆSTHESIA

Avertin or paraldehyde as a general rule weaken the cough reflex for too long. They may, however, be administered to children who with their high metabolic rate throw off the effects more rapidly. For bronchography I have given children 0·15 grm. of avertin per kilo of body-weight; this dose has produced sufficient unconsciousness to permit cocainization of the deep pharynx and the introduction of an oral endotracheal tube down which the lipiodol is run.

INTRAVENOUS ANÆSTHESIA

Apart from the occasional use of nembutal before spinal anæsthesia I have used pentothal sodium exclusively. I have seen no ill-effects follow the giving of the latter drug to patients who have had sulphonamide preparations. Pentothal sodium may be given continuously as a complete anæsthetic, or in a single injection for the induction of anæsthesia. The important point to remember about this drug is that it depresses the respiratory centre to a far greater extent than it decreases reflex irritability as shown by the laryngeal or the cough reflex. If pentothal sodium is given continuously during the drainage of a lung abscess there is considerable risk of the patient either coughing and then going into intense laryngeal spasm, or else developing a paroxysm of coughing which will produce intense dyspnœa and may rupture the abscess into the bronchial tree—vicious circle coughing once more. For the same reason it is unwise to attempt bronchoscopy under pentothal anæsthesia *alone*. Too often if the patient is light enough to breathe efficiently his reflexes will still be active, whereas if his reflexes have been abolished he will no longer be breathing—and one cannot inflate the lungs with a bronchoscope in place. Occasionally I intubate patients under pentothal anæsthesia without previous cocainization. Then I either keep the patient breathing until his laryngeal reflex has been subdued by giving him a CO_2 and oxygen mixture; or else I

CORRIGENDUM

PRINTER'S ERROR:

Proc. Roy. Soc. Med., 34, 492 (Section of Anæsthetics, p.14). Lines 7 to 9 *should read* ". . . . If respiration is depressed or abolished by the injection, I produce an efficient tidal exchange by gentle bag pressure, . . ."

inject enough pentothal to make certain that this reflex is well and truly abolished, and ignore the respiratory arrest during the half minute it will take to intubate the patient. Both these methods—though useful on occasion—cannot be recommended for general use.

I have used up to half a gram of pentothal very frequently for inducing anæsthesia in chest surgery. In the past I would never induce anæsthesia in ill patients with pentothal. Recently I have changed my views. I am now of the opinion that a *small* dose will not harm a patient so long as an efficient respiratory exchange is maintained. If respira- breathing bag should be only just sufficient to produce the requisite tidal exchange, and gentle bag pressure, and as a matter of fact I carry straight on with cyclopropane. In chest surgery distension of the lungs by excessive bag squeezing is contra-indicated and in light anæsthesia, at any rate, would make the patient cough. The hand pressure of the breathing bag should be only just sufficient to produce the requisite tidal exchange, and in contrast with positive pressure anæsthesia this low pressure is exerted only during the inspiratory phase of respiration. If the patient is ill and the operation is only likely to take a short time it is often better not to use pentothal because efficient respiration may not have returned by the time the patient is due to leave the theatre. It is frequently stated that if respiration is depressed under continuous pentothal anæsthesia, coramine and such like drugs should be injected to stimulate the respiratory centre. Surely it is better in such circumstances to carry on passive respiration until the pentothal has been detoxicated—this treatment will produce an instantaneous improvement in the patient's condition without the possibility of any side-effects.

THE USES OF CARBON DIOXIDE

For reasons already mentioned I usually employ some rebreathing for a minute or two during induction; and I may even add a spurt of CO_2 from a cylinder. If the patient is acidotic, however, or responds to a rise in CO_2 by rapid shallow breaths (or if he develops a tracheal tug) I put in a soda-lime canister at once and increase the tidal exchange by bag pressure. Although high concentrations of CO_2 depress both the respiratory and cardiovascular systems, a mild rise in CO_2 has usually two different actions. The one is central—stimulating the respiratory and the vasomotor centres—and the other peripheral—dilating the capillaries. Its central action may be helpful for brief periods—as during induction. When the canister is put in at the start, respiratory obstruction is more likely to occur because induction is slower; with an obstructed airway besides having a raised CO_2 the patient will be short of oxygen as well. During maintenance of anæsthesia, however, a raised CO_2 does not help the patient and I favour the CO_2 absorption technique. During recovery the use of CO_2 may be treacherous since the hyperpnœa produced may pull the anæsthetic out of the brain so fast that although the patient may react and appear self-supporting he may subsequently lapse back into deep unconsciousness as a result of spread of the anæsthetic from the tissues back into the brain (figs. $4c \rightarrow 4b$).

INHALATION ANÆSTHESIA

NITROUS OXIDE.—Nitrous oxide is the weakest anæsthetic we possess and without restricting the oxygen intake it does not produce deep enough anæsthesia for chest surgery. Magill in the paper already referred to said: "I am convinced that alternate bouts of cyanosis and oxygen inflation are unlikely to enhance the prospects of cure in patients suffering from pulmonary disease." Although when it is administered with adequate oxygen, nitrous oxide may be the least toxic anæsthetic agent, this is far from being the case when the required depth can only be obtained by cutting down the percentage of oxygen. Chest patients do best with a high oxygen percentage in the anæsthetic mixture. Therefore nitrous oxide is not the best agent for patients whose respiratory physiology is already handicapped. Even when anæsthetizing normal patients I am not in favour of reducing the oxygen intake to below that to which the patient is accustomed. I never give nitrous oxide unless about half the required depth of anæsthesia is produced either by premedication or by some supplementary drug. It should not really be called nitrous oxide anæsthesia at all but morphine and nitrous oxide; morphine, pentothal and nitrous oxide; or morphine, nitrous oxide and chloroform anæsthesia. The only indication, in my opinion, for using such a combination in chest surgery is when the diathermy knife must be used within the pleural cavity, for the welfare of the patient and not for the convenience of the surgeon. On other occasions I think that the best interests of the patient are served by using a high oxygen atmosphere with cyclopropane

(or ether) and dispensing with the diathermy current once the vessels in the chest wall have been sealed off—which may be done safely in spite of the explosive bag contents so long as the absorption technique is being used.

The diathermy knife, however, will save the patient much loss of blood during the closure of a tuberculous empyema ; and its use will also prevent blood from entering the bronchial tree when the track of a chronic sinus has to be followed and excised during the late removal of a retained foreign body from the lung.

CHLOROFORM.—This drug is considered to be too toxic to be used as the sole anæsthetic agent for patients who have had prolonged toxæmia. If the experimental work were redone to-day, taking care to produce smooth anæsthesia with a clear airway and excess oxygen, the toxicity would probably be much less. Apart from using it as an amnesic during thoracoplasty under local anæsthesia and as an adjuvant to nitrous oxide I have done a few thoracotomies on controlled respiration with this agent. The patients' condition—though satisfactory enough—was not as good as I had come to expect after cyclopropane. One patient developed a sharp attack of ventricular tachycardia.

ETHER.—I have had no experience with vinesthene in chest work. I have done pneumonectomies and lobectomies with diethyl ether but in most cases I prefer the flexibility of cyclopropane. When I am going to use ether for maintenance I always induce anæsthesia with cyclopropane. For those who have no cyclopropane or are unfamiliar with its use I would suggest that ether and oxygen would be the agent of choice for thoracotomy in war casualties. *Controlled respiration is the vital factor in dealing with many of these cases,* and the agent used with it is only of secondary importance. However, it is much easier to produce controlled respiration with cyclopropane or chloroform than it is with ether or nitrous oxide. Though it is often stated that ether should never be used for patients with pulmonary disease, yet Churchill uses ether for all his thoracotomies and even for thoracoplasties when active phthisis is present; perhaps the CO_2 absorption method has something to do with his good results.

On four occasions when I have been giving cycylopropane preceded by omnopon gr. $\frac{1}{3}$ and scopolamine gr. $\frac{1}{150}$ or this and pentothal sodium, either the breathing has become very shallow (as if inspiration had been cut off short), or, if the patient has already been in respiratory arrest, I have been unable to produce an efficient respiratory exchange with reasonable hand pressure on the breathing bag. The introduction of ether vapour almost at once increased the depth of respiration or allowed me to produce the requisite tidal exchange with my normal gentle bag pressure. All four were cases of carcinoma with bronchial stenosis and all four subsequently proved inoperable because of extension of the growth towards, or glandular involvement near, the hilum. The cause of the trouble seemed to be due to bronchiole spasm or a hyperactive Hering-Breuer reflex: thereby illustrating the vagotonic effect of cyclopropane in contrast to the sympatheticotonic action of ether.

CYCLOPROPANE.—Five years ago Magill gave as his considered opinion that cyclopropane was a godsend in surgery of the chest and he went on to say: "I feel certain that the operator who is able to forgo the advantages of diathermy in favour of the atraumatic anæsthesia which cyclopropane provides is amply repaid for his concession." Once inside the chest the surgeons with whom I work no longer use the diathermy needle except in the type of case that I have already mentioned. Presumably they agree, therefore, that the post-operative condition of their patients justifies this concession.

Unlike ether, cyclopropane depresses respiration much more than it decreases reflex irritability—as shown by disappearance of the laryngeal reflex and abolition of reflex tightening of the abdominal muscles. One's aim during any anæsthesia is to abolish reflex irritability and the depth of anæsthesia required for this will vary with the physique of the patient and the nature of the operation. In order to produce this state of affairs with cyclopropane which is such a potent respiratory depressant one has, in the average case requiring deep anæsthesia, to work at a level of narcosis far below respiratory arrest. If the patient is not robust, if one is prepared to take a long time inducing anæsthesia, if one is content with imperfect muscular relaxation, or if one uses little or no morphine beforehand, it is possible to maintain active respiration during abdominal operations, but I myself almost invariably use controlled respiration. About two years ago I had the privilege of watching Guedel in Los Angeles produce the most perfect muscular relaxation for upper abdominal surgery with cyclopropane. During the next twelve months I anæsthetized most of my upper abdominal cases with cyclopropane—preceded

by omnopon gr. $\frac{1}{3}$ and scopolamine gr. $\frac{1}{150}$ and sometimes by pentothal as well—and worked in a deep apnœa with controlled respiration. At the end of this trial period I reverted to the use of a field block with light inhalation anæsthesia since I was dissatisfied with the slow return of full consciousness from very deep cyclopropane anæsthesia ; the fact that one had to use a high concentration of cyclopropane towards the end of a long operation for closing the peritoneum was responsible for this delay in recovery. This year's experience, however, made me familiar with deep cyclopropane anæsthesia and controlled respiration.

When I first applied this method to war chest casualties I was pleased to note that the important differences between reflex irritability in the chest and that in the abdomen made cyclopropane an excellent agent for thoracic surgery. Although stripping the periosteum from the ribs is a very stimulating procedure and one likely to set up laryngeal spasm if the depth of anæsthesia is inadequate, the depth required in order to open the chest without reflex response is considerably less than that necessary to open the abdomen in comfort. Again, although patients may dislike the surgeon working on the upper surface of the diaphragm almost as much as they object to his handling the mediastinum, all reflex disturbance from this is abolished at a lighter degree of anæsthesia than is the stimulus produced by exploring the abdomen. Finally, once the surgeon has finished work near the diaphragm and the hilum the depth of anæsthesia can be reduced and closing the chest, in contrast to the abdomen, does not require deep anæsthesia. I do not hesitate, therefore, to produce deep anæsthesia at the requisite times since I know I would use a higher concentration for abdominal surgery, and I can always arrange for the patient to be awakening at the end of a chest operation. Provided the airway is clear and an efficient respiratory exchange is maintained I do not regard deep cyclopropane anæsthesia as more harmful than light. With cyclopropane—just as with all other agents—a somewhat deeper anæsthesia than that actually required is safer than a depth only slightly too light.

Apart from having to work below respiratory arrest when deep anæsthesia is required anæsthetists also worry about the cardiac arrhythmias which may occur during the administration of cyclopropane.

Occasional extrasystoles may appear when a patient is breathing very shallowly ; although he has at the time an excellent colour these commonly disappear as soon as a more efficient respiratory exchange is produced by bag pressure and these are, in fact, seldom observed if the tidal exchange is always kept adequate. Regular extrasystoles or pulsus bigeminus may be observed not infrequently in deep anæsthesia. Guedel (1940) wrote at length on the subject of arrhythmias in the first issue of the journal *Anesthesiology*. He maintains that there is an area in cyclopropane anæsthesia during which arrhythmias may occur. He believes these arrhythmias to be non-toxic in origin since by increasing the depth of anæsthesia he is able to pass through them and get back to a normal regular pulse once more (and I have watched him do it). The width of this arrhythmic area and the depth at which it manifests itself will vary with different individuals. Young, robust, or nervous patients are more likely to develop arrhythmias than are elderly, feeble, or placid individuals, and in the former groups the arrhythmic area is likely to extend over a greater proportion of the anæsthetic range. Guedel believes that cyclopropane lowers the threshold of irritability of the cardio-neuro mechanism and that the previous use of barbiturates—such as evipan or pentothal sodium—will counter this by their opposite effect on the threshold. While the effect of pentothal sodium lasts he reckons it provides 90% protection against the appearance of arrhythmias. I very commonly use pentothal sodium for induction and have not encountered arrhythmias on many occasions. Recently a boy of 17 to whom I had given half a gram of pentothal sodium had a wildly irregular pulse during the greater part of a thoracotomy, which took half an hour. His peripheral circulation remained unaffected and normal rhythm had returned by the conclusion of the operation. This boy had a very wide arrhythmic area and it was not worth going below it for a short operation because the arrhythmia would have almost certainly returned as the depth of anæsthesia lightened; nor was it practicable to add oxygen to decrease the cyclopropane concentration and come out above the arrhythmic area because he would by then have been too lightly anæsthetized and would have probably developed laryngeal spasm. Under cyclopropane anæsthesia respiratory obstruction and anoxia *must* be avoided at all costs. After watching Guedel, a ventricular tachycardia under cyclopropane—provided the airway is clear and the peripheral circulation remains good—does not frighten me like a similar condition under

chloroform—because the latter I consider is almost certainly toxic in origin. I have never seen a ventricular tachycardia occur after a rapid induction although a bradycardia is common. Provided that one does not try to deepen anæsthesia too quickly later on—for instance when the surgeon suddenly decides to close the abdomen before one expects him to—I do not think arrhythmias will often occur. Patients who require chest surgery are seldom the type who are likely to develop arrhythmias.

I am in favour of a rapid induction with cyclopropane, but I have given up the practice of filling the bag with equal parts of cyclopropane and oxygen because every now and then a 50% concentration of cyclopropane irritates the larynx. Then, instead of induction of anæsthesia taking a couple of minutes, it will be interrupted by laryngeal spasm. Whenever the larynx has once been irritated, directly or reflexly, the subsequent anæsthesia has to be more profound than would have been necessary had this reflex never been insulted. During chest surgery I intend to use controlled respiration and therefore set out to depress the respiratory centre. Most adult patients receive a hypodermic injection of omnopon gr. $\frac{1}{3}$ and scopolamine gr. $\frac{1}{150}$ one and a half hours before operation and frequently also up to half a gram of pentothal sodium intravenously. I start with the canister out as a rule and allow the patient to rebreathe into a bag half-filled with oxygen. If respiration is depressed I augment the exchange with gentle bag pressure and run in, say, 800 c.c./min. cyclopropane with, say, 1000 c.c./min. oxygen. The rebreathing usually maintains respiration because the rising CO_2 keeps pace with the depression of the respiratory centre; if it does not I gently squeeze the bag rhythmically by hand. After about a minute one can usually insert a pharyngeal airway with ease. I use a Waters's airway smeared with Brennan's 10% percaine paste. When an endotracheal tube is to be passed I carry on for another minute or so, although the patient probably will not now be breathing on his own ; if the patient is very robust I allow the cyclopropane and oxygen to pass over the surface of a small ether bottle because this will then allow plenty of time for laryngoscopy and fixing up the apparatus without the patient reacting on the tube. As soon as the pharyngeal airway is inserted, or the endotracheal tube is in place, I insert the soda-lime canister. The CO_2 falls to normal and apnœa—if not already present—results, and I then carry on with controlled respiration about twenty times per minute. I watch the pulse and peripheral circulation closely during induction and can tell from the feel of the bag in my hand when the larynx will permit an easy intubation. With a rapid induction like this, especially when pentothal has been used as well, one is on a very uneven keel because one has a high brain saturation and next to no tissue saturation at all (fig. 4*a*). One must therefore go on adding more cyclopropane to compensate not only for spread of the cyclopropane from the brain to the tissues but also to replace the pentothal which is being detoxicated. When using a pharyngeal airway I commonly add 500 c.c./min. cyclopropane and 500 c.c./min. oxygen—supposing the basal oxygen consumption were 250 c.c./min. this would represent adding this quantity of cyclopropane at a concentration of 66% to the bag mixture. This flow is left running until I am certain that the larynx will continue to remain wide open when the chest is entered. Thereafter the flow is progressively cut down or the basal oxygen left running alone. It is easy to detect the first sign of laryngeal irritability by the feel of the bag. Should this occur and the concentration of cyclopropane is high a spurt of oxygen will often clear up the trouble. If this fails the depth of anæsthesia is too light.

How can one tell the depth of anæsthesia when one is using controlled respiration? This is not difficult after a little practice and may be determined in two different ways. When the patient is in a light apnœa and the bag squeezing is discontinued for half a minute or so, active respiration will return as a result of the banking up of CO_2 and from the character of the breathing the depth of anæsthesia can be ascertained. Alternatively, the canister can be "cut out" and a spurt of CO_2 added to the bag, if after a few squeezes of the bag active respiration is resumed once more one can determine the depth ; if the breathing remains in abeyance, however, it is obvious that the patient is in a deep apnœa since the respiratory centre is out of range of stimulating concentrations of CO_2. In the latter event, after the canister has once more been "cut in", one can possibly afford to lighten the depth of anæsthesia so long as reflex irritability, as shown by the larynx or other reflex response, does not appear.

I do not now fit a by-pass to the soda-lime canister, and once induction has been completed it is a nuisance to take the canister out and put it back again. I therefore rely on a different method of determining the depth of anæsthesia which although it may not be

scientific works well in my hands. I simply let a little of the anæsthetic mixture out of the tail of the bag and smell it. With a little practice it is not difficult to recognize different concentrations of cyclopropane. If one's sense of smell detects a concentration of, say, 40-50% the patient is obviously in a deeper apnœa than if it was 20-30%. If one can smell next to no cyclopropane at all the apnœa is due almost entirely to a low CO_2 (unless too much premedication is responsible for depression of the respiratory centre). After a little practice one knows pretty well from the type of patient, from his response to the pre-anæsthetic drugs, from his behaviour during induction, from the feel of the bag, and from the course of the operation, what concentration of cyclopropane will be required to abolish reflex irritability. The eye signs may be helpful at times and, of course, the cardiovascular system must be watched throughout.

Resort to either of these methods will save the anæsthetist from two embarrassing situations. Supposing, for example, he does not add sufficient cyclopropane during the early part of the operation to make good the spread from the brain to the tissues or sets the basal oxygen too high, the cyclopropane concentration in the brain will obviously fall. That, one might imagine, would make active respiration return once more, and so it should ; but supposing the anæsthetist has by mistake been hyperventilating the patient the CO_2 will be low and the breathing may remain absent for this reason although the patient is obviously too lightly anæsthetized. Before I realized this I used to find every now and then that the patient—although still apnœic—was lighter than I had expected and he might even react on an endotracheal tube or develop laryngeal spasm. A similar state of affairs occurs also when a conscious patient is hyperventilated until he has no desire to breathe. A study of Guedel's stimulus and threshold board will help to make my meaning clearer (Nosworthy, 1939).

The other embarrassing situation is when the anæsthetist does not realize until the operation is nearly over and active breathing is due to return that the patient is in a deeper apnœa than he expected, and consequently he has to keep the patient in the theatre until he has got rid of the unnecessary excess of cyclopropane and restored normal breathing.

Neither of these troubles will arise if the anæsthetist keeps a mental picture of the principles upon which controlled respiration depends. Smelling the mixture every now and then, and the following additional points will help to keep him straight. Whenever it is necessary to add cyclopropane during the operation always increase the basal oxygen flow enough to prevent the building up of too high a concentration ; for instance, if 500 c.c./min. of cyclopropane is added, put the basal oxygen up, say, another 250 c.c./min. which means that however long it is left running the ultimate concentration cannot exceed 66%. If the system leaks so that the bag volume is lost replenish it with the same mixture that it contained before ; for instance, if there was 30% cyclopropane in the bag mixture previously, turn the cyclopropane up to 600 c.c./min. and the oxygen up to 1,400 c.c./min. Finally, remember that the longer the operation has been in progress the lighter the degree of anæsthesia can be.

I lighten anæsthesia in major chest cases performed during quiet times by putting the basal oxygen up to 500 c.c./min. while the chest wall is being closed. It is seldom necessary to remove the canister to get the patient to resume breathing on his own. The effect of the omnopon-scopolamine and the pentothal will have worn off so that it is only necessary to wash out the cyclopropane. I bring these patients out in a high oxygen atmosphere because it is always possible, and usually desirable, to give oxygen therapy for a few hours post-operatively. The B.L.B. mask should be applied in the theatre so that the patient cannot get short of oxygen during his transfer to the ward. In a rush of war casualties, however, I lighten anæsthesia by switching over to nitrous oxide during the later stages of the operation. By this means I can forecast which patients *must* have post-operative oxygen, and I have not been troubled by circulatory depression after operation.

I see no indication for the use of helium except in the presence of respiratory obstruction due, for instance, to an acute asthmatic attack, or to laryngeal or tracheal obstruction caused by a thyroid tumour. I wish that I had had it to try on the four cases with bronchial stenosis to which I referred earlier on. If an inert gas is all that is required I can see no practical advantage in helium over air, which is cheap and readily available. When the effective lung area is small it is more beneficial to raise the oxygen percentage than to introduce helium into the anæsthetic mixture.

PHARYNGEAL AIRWAY OR ENDOTRACHEAL TUBE ?

Now we come to the question of whether chest cases should be intubated or not. There are two reasons for endotracheal anæsthesia, firstly to provide for the removal of secretions by suction, and secondly to maintain a clear airway. When copious sputum is present or likely to appear intubation, in my opinion, is essential. When the anæsthetist is uncertain whether he will be able to maintain a clear airway throughout the operation the patient is safer intubated. The presence of laryngeal spasm will soon destroy the patient's chances of recovery from a chest operation. For this reason until the anæsthetist has become thoroughly at home with controlled respiration he will have more peace of mind if the vocal cords are propped open by an endotracheal tube.

The great majority of our war casualties have had no hæmoptysis at the time of operation and not too much sputum, and I have just used a pharyngeal airway during thoracotomy. The patient can then be placed in the lateral position before induction and the surgeon can start almost at once since deep anæsthesia is not required until the periosteum is stripped. Provided the results are satisfactory a technique which saves time is one to cultivate in war ; Brock and I in this way completed five, admittedly short, chest operations, and were in and out of the theatre in seventy-five minutes.

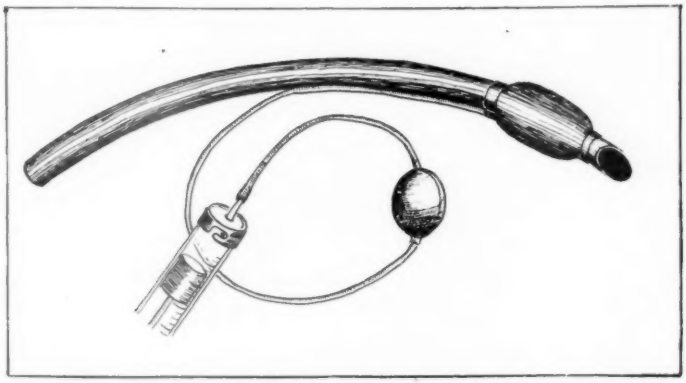


FIG. 5.—Balloon endotracheal catheter fitted with small tell-tale balloon.

I intubate patients who have a quantity of sputum under local anæsthesia, or local anæsthesia followed by pentothal sodium. Patients in the wards with secretion which they cannot get rid of—perhaps on account of fractured ribs—may be intubated "blind" while propped up in bed after a tablet of decicain and a spray with cocaine. The suction catheter can then be passed down the lumen of the endotracheal tube. A larger tube can be passed through the mouth than through the nose, and therefore I always do a direct vision oral intubation whenever I use endotracheal anæsthesia for chest cases. I am in the habit of using a balloon catheter (figs. 5, *6d* and *9a*) ; such a tube must not be too long or a one-lung anæsthesia will result. It is important not to distend the balloon on the catheter too tightly because this will necessitate a deeper depth of anæsthesia and may interfere with ciliaf action subsequently. The usual practice is to inflate the balloon until resistance is felt on the plunger of the syringe and then to inject another c.c. A better method shown me by Guedel is to squeeze the breathing bag during the inflation of the balloon and to stop as soon as the system is airtight ; by this means perhaps 3 c.c. less air will be required which is obviously all to the good.

PNEUMONECTOMY

A one-lung anæsthesia is ideal for pneumonectomy for the following reasons. Secretions and blood cannot get across and infect the sound lung. The surgeon should have a collapsed lung to work on. Efficient ventilation can be secured in spite of the presence of a bronchopleural fistula on the affected side. This technique can be carried out in two ways. In the one an endotracheal anæsthesia is given after blocking the

bronchus on the affected side with a balloon or a strip of gauze plugging. Crafoord uses bronchial tamponage for both pneumonectomy (fig. 6*b*) and lobectomy (fig. 6*c*). With the other method the breathing tube is placed in the sound bronchus and endobronchial anæsthesia is given. There are a number of anatomical points which must be appreciated in order to secure a successful endobronchial intubation. I am much indebted to Norman Barrett for the diagrams which he has drawn to illustrate the troubles which will result from a faultily placed tube.

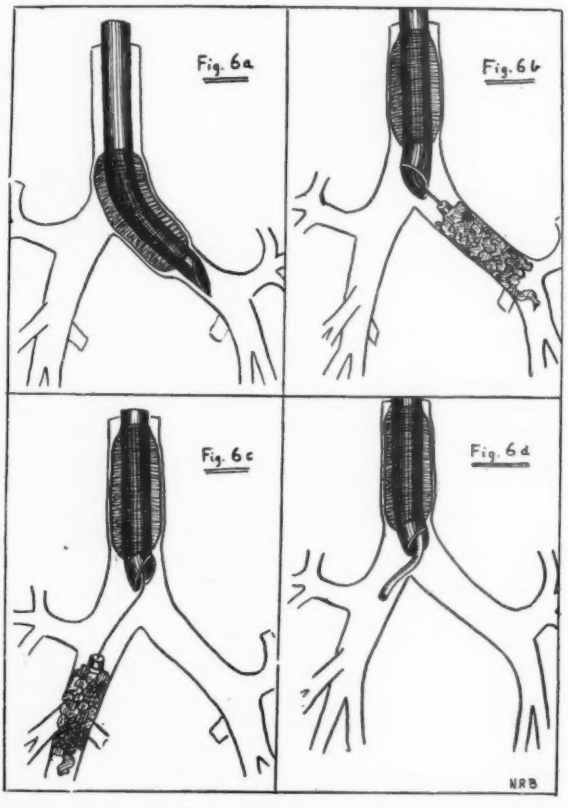


FIG. 6 (*a*).—A left endobronchial intubation with balloon occluding orifice of right main bronchus. (*b*) Left bronchus blocked by ribbon gauze packing kept in place by wire rod over which endotracheal catheter is threaded (for left pneumonectomy—Crafoord). (*c*) Crafoord's technique for right lower lobectomy leaving upper lobe bronchus patent. (*d*) Destination of tip of suction catheter uncertain when passed down endotracheal catheter.

The normal angle of deviation of the right bronchus is about 25° whereas that of the left is about 75° (fig. 7). If it is passed on blindly through an ordinary laryngoscope an endotracheal tube of sufficient length will therefore normally enter the right bronchus in preference to the left. Pathological conditions in the chest, however, may very considerably distort the bronchial tree either by displacement of the trachea, or by alteration of the angles of deviation of the bronchi. Fig. 8 shows the different distortions which result from atelectasis in the various lung zones. A neoplasm of the lung, bronchiectasis,

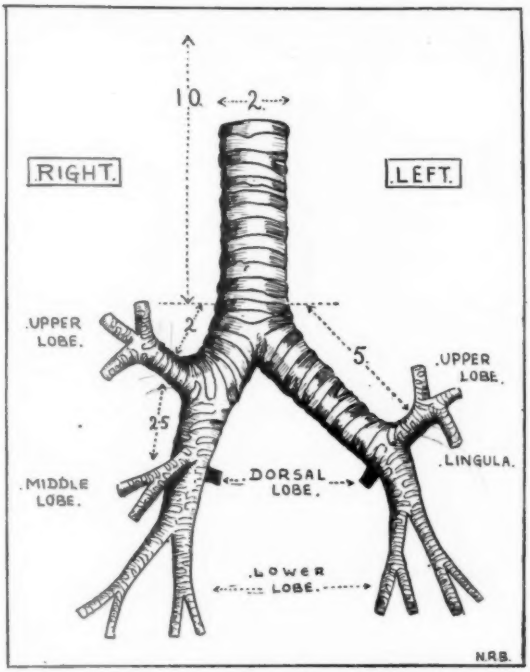


FIG. 7.—Anatomy of the normal tracheobronchial tree.

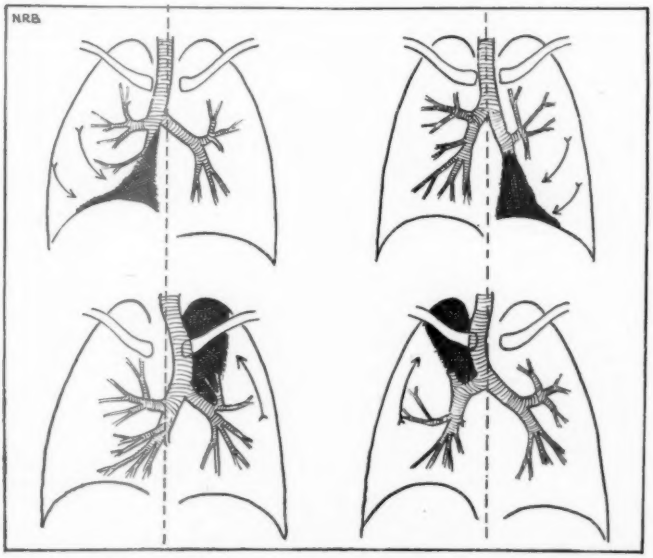


FIG. 8.—Distortion of the tracheobronchial tree due to atelectasis in different lung zones.

or an artificial pneumothorax will also alter the normal angle of deviation of the bronchi. Before deciding upon blind bronchial intubation the anæsthetist must therefore examine the X-ray films in order to ascertain whether such a procedure is a practical proposition or not. Even after the tube has gone down the correct bronchus his troubles are not ended. Although the right bronchus is 1·5 cm. in length the superior border of the mouth of the upper lobe bronchus is at the level of the carina. The significance of this is that although it may be easy as a rule to intubate the right bronchus blindly it is also easy to occlude the orifice of the upper lobe bronchus (fig. 9*d*), in which case the patient will be left

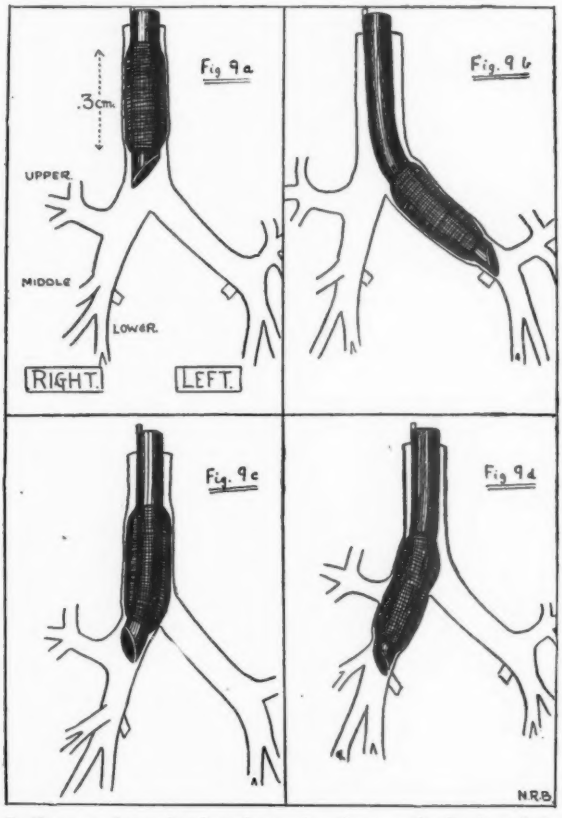


FIG. 9 (*a*).—Balloon endotracheal catheter in place. (*b*) Perfect left endobronchial intubation—ideal for right pneumonectomy (compare with fig. 6*a*). (*c*) Right endobronchial intubation with balloon occluding orifice of left main bronchus. (*d*) Right endobronchial intubation with balloon occluding right upper lobe bronchus.

breathing on two lobes only and will become cyanosed. If the bevel of the tube is facing its orifice the risk of occluding the upper lobe bronchus will be decreased (fig. 9*c*). Having inflated the balloon after such an intubation I listen with a stethoscope to make certain that the airway to the upper lobe is clear. There is not room for the balloon to be entirely accommodated in the right bronchus and if it distends and fills the lower end of the trachea (fig. 9*c*) air will be trapped in the left lung—unless a complete artificial pneumothorax has been produced beforehand. In such an event there will be a circulatory "shunt" since blood will continue to circulate in the uncollapsed left lung, and since this

blood will not be oxygenated the patient will become cyanosed. Of course once the pleura is opened the left lung will collapse if the balloon filling the lower end of the trachea is momentarily deflated ; but on blowing it up again the chances are that the tip of the tube will have slipped out of the right bronchus back into the trachea.

I have been fortunate in a fair proportion of blind right bronchial intubation but I have never succeeded in getting round the corner and intubating the left bronchus blindly. This bronchus, however, is 5 cm. long and once the tube is in the correct bronchus there is more margin for error since there is less risk of occluding the left upper lobe bronchus (figs. 9*b* and 6*a*). For a child it is better not to use a balloon catheter for endobronchial anæsthesia but to select an ordinary endotracheal tube of a size which one judges will be a plug fit in the bronchus ; such a tube will give the child the maximum airway through which to breathe. From all this it will be appreciated that successful blind bronchial intubation is an undertaking in which chance plays altogether too big a part.

To permit accurate placing of an endobronchial catheter I have a 9 mm. bronchoscopic tube over which is slipped a Magill balloon catheter. Local anæsthesia is used in the same way as for bronchoscopy. It is important to anæsthetize the bronchial mucosa, otherwise the presence of the endobronchial tube may cause bronchial spasm and cyanosis once more. Before passing such a tube blindly I always smear over the balloon Brennan's 10% percaine paste, and do not attempt the intubation until I have produced the deepest possible apnœa. Placing of the tube should be much more accurate by direct vision under local anæsthesia. Bronchoscopy in expert hands is a simple procedure. As soon as the tube is in place the balloon is inflated and the bronchoscope withdrawn.

In one recent case which after thoracotomy turned out to be inoperable—all went well until the skin was being sutured ; then the patient coughed and pushed the tube from his left bronchus back into the trachea. Perhaps the answer to a successful endobronchial anæsthesia may lie in a silkwoven or gum-elastic catheter introduced under direct vision. Such a catheter should retain its position better than the soft rubber Magill tube. I also want to try a rather floppy balloon 3 cm. in length. A successful endobronchial anæsthesia works so well that I feel that with further experiment this method will work smoothly every time.

Although a one-lung anæsthesia is ideal, in my opinion, for pneumonectomy or for the repair of a diaphragmatic hernia (when attacked through the chest) I have done both with endotracheal anæsthesia which works well enough in many cases. Of course, an endotracheal anæsthesia should always be used if there is uncertainty as to whether a pneumonectomy or only a lobectomy is to be performed. If an endotracheal anæsthesia is to be used for a patient with bronchial stenosis or an artificial pneumothorax I now always perform the intubation under local and pentothal anæsthesia, and do not put the patient into controlled respiration until the pleura has been opened and I can see what is happening to the underlying lung.

I think it is advisable to induce an artificial pneumothorax before deciding upon pneumonectomy in an elderly patient. If the patient becomes dyspnœic after the induction or the refills, it is well to wait until he gets accustomed to breathing on one lung. If the dyspnœa does not disappear or the air is rapidly absorbed, it may point to emphysema of the other lung or to his need for what alveolar tissue remains in the diseased lung. In such circumstances although he would probably survive the operation the chances are against his walking out of hospital. The vital capacity should also be taken before and after the production of the artificial pneumothorax.

When the surgeon is working inside the chest and everything is going well under a sufficient depth of anæsthesia the chief points to be attended to are efficient—but not excessive—ventilation with excess oxygen, the state of the cardiovascular system, and the rate of the blood transfusion. I have already mentioned that a local anæsthetic injection into the hilar region is helpful. Sometimes when the surgeon is dealing with the bronchus one may suddenly find oneself unable to produce any tidal exchange owing to his having distorted the tracheo-bronchial tree. In my experience this respiratory obstruction has been due to accidental rotation of the handle of the bronchus clamp, and the surgeon will free the airway as soon as his attention is called to it. This momentary mishap, however, has usually been sufficient to produce secretion which can be easily sucked away so long as the patient has been intubated.

I like the patient to attempt to breathe on his own once or twice during the later stages of the operation because this will confirm my estimation of the depth of anæsthesia. Active thoracic breathing is not allowed to return until the chest wall is nearly closed. The

breathing tube should not be removed until the patient has been bandaged up and placed on his back, and during its withdrawal a suction catheter should be passed to make certain that the air passages are left quite clear. The B.L.B. mask is then strapped in place. The blood transfusion is replaced by a saline infusion, which is set at a rate just sufficient to keep the vein patent and is left dripping for twelve hours or so. A brisk post-operative hæmorrhage which occurred in one of our cases suggested the advisability of this safeguard ; there need now be no delay in replacing any lost blood by a further transfusion. It is also useful from my point of view in that morphine, which is usually required almost at once, can be withheld until the psychological moment and then can be injected into the rubber tubing of the infusion, the rate of which is momentarily speeded up.

LOBECTOMY FOR BRONCHIECTASIS

Lobectomy is a much less severe operation and is commonly performed on younger and fitter subjects than pneumonectomy. When the patient has much sputum, however, the anæsthetist has to cope with the difficult problem of preventing the secretions from spreading to other parts of the lungs. Spinal anæsthesia is satisfactory in some cases but is far from being the ideal method. A one-lung anæsthesia, in my opinion, is unsound since there is nothing to stop secretions in the affected lobe from being squeezed into the

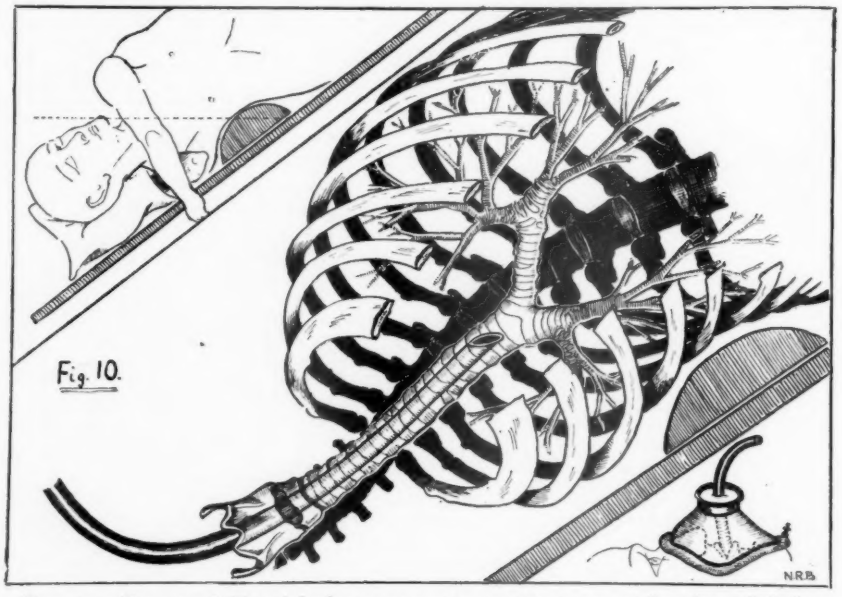


FIG. 10.—Degree of Trendelenburg necessary to prevent secretion from left lung running into right bronchial tree. When the endotracheal tube is not fitted with a balloon sputum will not be dammed back near the carina.

normal parts of that lung. An endotracheal anæsthesia with a balloon suction catheter in the bronchus of the affected lower lobe is ideal provided that the balloon can be placed and retained with certainty in the right place. Should the balloon become displaced back into the main bronchus, however, suction through the catheter may cause atelectasis of the remainder of the lung on the affected side. If the tip of the suction catheter only extends to the bifurcation of the trachea it may not evacuate all the sputum, and the necessity for suction may be appreciated just too late. When it is necessary to suck out secretion through a bronchoscope at the conclusion of the operation the anæsthetic technique must be regarded as far from perfect. Magill will show you some of his instruments with which to block off the diseased portion of the lung but few, if any,

possess his manual dexterity. Without one of these techniques I frankly admit that I do not know how *all* risk of post-operative trouble can be eliminated. Even though spread of infection may be a rare occurrence, one should not sit back and be content with an anæsthetic technique with which one cannot guarantee absolute protection.

When the technical difficulties associated with an ideal but complicated method are so great that the chances of success with it are small, there is much to be said for using a simple though far from ideal method *until* such time as a better one has been worked out. Beecher just uses a wire coil endotracheal catheter and maintains an airtight fit not by a balloon but by bringing the end of the catheter out through a rubber diaphragm fitted to the top of a rubber facepiece (fig. 10). With this arrangement the sputum is not dammed back near the bifurcation of the trachea by the balloon but, with the patient in the Trendelenburg position, it is free to flow along the trachea and out into the facepiece. Thus when there is a sudden gush of pus the anæsthetist has not to evacuate all of it through the suction catheter which is passed down the endotracheal tube. Although suction may be required at other times Beecher applies it routinely at the following stages: after intubation, after the patient has been turned on his side, when the pleura is opened, when the lung is mobilized, when the tourniquet is applied, when the tourniquet is loosened, and on withdrawal of the tube at the end. Bronchoscopic suction at the conclusion of the operation may be necessary.

For " wet " cases there is something to be said for using such a " set-up " in preference to a balloon endotracheal catheter. Provided the apnœa with cyclopropane is sufficiently deep reflex response to suction is no more likely to occur with this agent than with ether. If one is using controlled respiration with such a technique and one finds that the bag pressure necessary to expand the lungs has suddenly increased one should not apply it but should regard it as an indication for suction, and possibly for increasing the depth of anæsthesia afterwards. Some patients can be permitted to breathe on their own and the paradoxical respiration satisfactorily overcome by slight bag pressure during the inspiratory phase only. I have found it useful to mark the suction catheter with a strip of sticking plaster ; this marker will indicate how deeply the catheter has been inserted. When a suction catheter is passed the mouth of the endotracheal tube should be open to the atmosphere in order to guard against the risk of deflating the lungs. It is a useful practice to lubricate the inside of the endotracheal tube with sterile paraffin before intubation when suction may subsequently be required ; sputum will then be less likely to stick to the tube and the suction catheter will slide in more easily.

BRONCHOPLEURAL FISTULA

Patients with a bronchopleural fistula are unpleasant to handle from the anæsthetist's point of view. One has only to notice how slight exertion quickly produces dyspnœa in a patient who has blown a fistula during convalescence from a pneumonectomy to realize that the presence of a fistula of any size prevents efficient respiration. In the presence of a large fistula controlled respiration cannot be established during operation, and the delivery of a large volume of gases—since a large fistula neutralizes any positive pressure—may do little to control the effects of an open pneumothorax. If the surgeon can plug the fistula he will assist the anæsthetist and prevent blood from entering the bronchial tree ; either because of its situation or because there is more than one fistula he seldom seems able to do this. Alternately plugging the fistula and then letting it open again helps the patient but little and the anæsthetist not at all. When pneumonectomy is to be performed it is well worth spending some time, if need be, on the intubation for a perfect one-lung anæsthesia. I have already mentioned methods of minimizing the dangers of draining an empyema associated with a bronchopleural fistula.

Although a war chest casualty has a foreign body in his lung there is frequently no demonstrable bronchopleural fistula—the hole in the lung having been rapidly sealed off. If one slowly loses one's bag volume and one believes that the leak is due to a small bronchopleural fistula, one must remember that in a war casualty it will be a bronchocutaneous fistula, and the use of the diathermy needle even on the chest wall may, therefore, be dangerous with an explosive anæsthetic agent. Whenever I give nitrous oxide by the absorption method I always keep 500 or so c.c./min. running in order to wash out nitrogen as it is eliminated. With a small fistula this may be sufficient but the volume of nitrous oxide must be governed by the size of the fistula and sufficient cyclopropane, ether or chloroform added to maintain quiet respiration—if the fistula is too large to permit controlled respiration. Quiet breathing, which is essential in my opinion, is

secured more safely in this way than by larger doses of premedication because one wants the depth of anæsthesia to be under one's control and also a rapid recovery afterwards.

War Chest Casualties

Physical examination and X-ray pictures are essential in war casualties. One man had a collapse of the right lower lobe and a right pneumothorax without any external injury (X-ray). Without physical signs and X-ray evidence in the early stages the diagnosis of "blast" is difficult to make. Some patients, however, require urgent operation before the possibility of blast can be excluded.

Although a simple hæmothorax is treated best by aspiration, with or without air replacement, patients with a compound hæmothorax frequently require operation because the blood has clotted, or in order to remove a foreign body, to secure a bleeding intercostal vessel, to close a sucking wound or to remove shattered rib fragments. By early operation normal physiological function may be restored and the patient saved from chronic infection in the pleural cavity or the lung. When the pleura is about to be opened during such an operation I wait with the patient in apnœa and my hand on the breathing bag. If the bag volume does not increase as it normally should when the pleura is opened, I keep in the back of my mind the thought that the lung on the affected side may be atelectatic—the significance of this I will explain later. I then resume controlled respiration and with gentle bag pressure rhythmically inflate the sound lung without, as a rule, causing expansion of the lung compressed by the hæmothorax. After twenty minutes or so the lung on the affected side seems to ungum itself and begins to expand on bag pressure. When the chest is about to be closed I apply *slightly* more pressure to the breathing bag and gradually bring the lung up to the surface, until by the time the chest is shut the pleural space has been obliterated. I time the controlled respiration so that the lung is falling away from the chest wall during the expiratory phase each time the surgeon is inserting a stitch. The intercostal catheter which is inserted for forty-eight hours is left open until the chest has been completely closed when after a full expansion of the lungs it is spigoted. On the patient's return to the ward the catheter is connected to an under-water seal without letting air into the pleural cavity; in this way normal respiratory function may be restored at once in many patients.

In one case in which I noticed on opening the pleural cavity that the lung on the affected side did not collapse further—as judged by the bag volume remaining unchanged—the result was as follows: With the bag pressure I am accustomed to use I could not re-expand the lung on the affected side. Exhorted by the surgeon, however, I finally managed to expand the lung fully but only by using heavy pressure on the breathing bag. An X-ray picture taken the next day showed the lung fully expanded but also a fluffy shadow which looked like a hæmatoma of lung. This subsequently liquefied and was coughed up, and the patient left hospital in six weeks with no physical or X-ray signs in his chest. If, however, a lung does not re-expand easily it may be safer to leave it collapsed at the time of operation.

Foreign bodies may be removed from the lung by various means. If it is near the surface the foreign body may be just nipped out. A wedge of lung may be resected with a knife between forceps; this is a longer and more elaborate operation but it makes a clean sweep of foreign body and all damaged lung tissue, and never makes a bronchopleural fistula. A lobectomy may be necessary. As already mentioned, the track of a chronic sinus may be burrowed out with the diathermy needle and the foreign body removed. Finally, special forceps may be passed through normal lung tissue and the foreign body pulled out under the X-ray screen. Much to my surprise no blood entered the bronchial tree on the only occasion we attempted to use this last method.

Thoraco-abdominal wounds are especially serious when the abdomen has to be opened as well as the chest. The repair of a hole in the diaphragm is made as easy as possible by controlled respiration. During operation for the few injuries to the heart and pericardium which we have had there has been no cause for anxiety—unless one regards as such the failure of all the theatre lights which occurred on one occasion!

War chest casualties are easy to handle—far easier, in my opinion, than the ordinary civilian sick with pulmonary disease. Even when they are very ill it is amazing how much they will stand inside the chest under controlled respiration. I do not think, however, that I am prejudiced when I say that several would probably have died on the table without controlled respiration. At operation we have actually lost one patient—death

being due to uncontrollable hæmorrhage from a hilar injury. The method which I have outlined—and for which I claim no originality—not only provides the best operative conditions that I have yet seen, but also good after-results which are equally important since many of these patients have to have subsequent operations.

Chest patients—especially if they have not received efficient early treatment—are prone to develop complications and it may be many months before results can be accurately assessed. Following the first 200 operative procedures performed by the Horton Chest Unit after the Dunkirk evacuation 12 patients died in hospital. Apart from the one patient who, as already mentioned, succumbed at operation, the remainder died at times which varied from a few hours up to eight months after their original injury or operation. Three patients with thoraco-abdominal injuries died, one from liver abscess, pulmonary suppuration, and empyema, and the other two from the extent of their injuries. Of two patients with sucking wounds and one or more other injuries, one improved for ten hours after operation and then died rather quickly, ? effect of blast; the other also died rather unexpectedly eight hours after operation. One patient who had multiple injuries died with acute dilatation of the stomach a few days after a massive secondary hæmorrhage. One patient died of pulmonary suppuration round his foreign body and bilateral empyema. Two patients died from a metastatic abscess, the one in the hip-joint and the other in the brain. Two patients died after pneumonectomy, one with pericarditis and the other with an empyema on the other side.

In conclusion, I would like to express my gratitude to the members of the surgical, medical, and nursing staff who have all helped me enormously. Co-operation between surgeon and anæsthetist is all-important. The more responsibility the surgeon places on his anæsthetist the more he will get out of that anæsthetist. If any reliance is to be placed on his opinion, however, it is up to the anæsthetist to increase his knowledge by seeing patients beforehand and by following their post-operative course. Anæsthesia should not begin and end in the operating theatre. Finally, I should like to take this opportunity of thanking Magill for all his help and encouragement to me in recent years.

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Discussion.—Mr. C. LANGTON HEWER agreed with Dr. Nosworthy on the extreme usefulness of cyclopropane in thoracic surgery. He thought that the alleged disadvantages of the gas were chiefly due to errors in the technique of its administration. For example, inefficient carbon dioxide absorption was not so obvious as with other anæsthetics and caused a rise in blood-pressure with consequent capillary oozing. Again, a sudden reduction of the oxygen percentage at the conclusion of the operation might lead to collapse. Mr. Hewer discussed the advantages of adding nitrogen from air to the anæsthetic mixture and of using cyclopropane as an adjuvant to nitrous oxide and oxygen.

In the adoption of controlled respiration was it certain that higher blood concentrations of anæsthetics than had previously been used were innocuous? The stage of overdose with paralysis of the respiratory centre was reached deliberately and life was maintained by artificial respiration. At least one fatality had already been reported while this procedure was being done with cyclopropane. After natural respiration had ceased it was extremely difficult to gauge if any acapnia was being produced by artificial hyperventilation. It should be remembered that Crafoord originally used controlled respiration because he asserted that during operations with open pleura, the carbon dioxide tension rose to a dangerous level which could not be lowered by natural respiration even when reinforced by positive pressure. H. K. Beecher repeated this work but could find no evidence of a dangerously high carbon dioxide tension with ordinary methods of inhalation anæsthesia. He also pointed out that even if this did occur, it was probably no more toxic to the patient than the alkalosis which may accompany prolonged acapnia during controlled respiration. There was, however, no doubt that the cessation of all respiratory movement while the surgeon was performing an intricate manœuvre inside the chest was a great advantage. The two other assets of controlled respiration were usually given as the abolition of paradoxical breathing and of mediastinal flap, but they were not so important as they could also be effected by means of positive pressure.

If spinal analgesia was used in thoracic surgery, Mr. Hewer thought that the unilateral technique with light percaine had definite advantages over the bilateral method. Since fewer anterior roots were paralysed, the fall in blood-pressure was not so great. Again, since most of the intercostal and abdominal muscles of the unaffected side still continued to function, coughing was more effective in evacuating sputum.

Mr. Hewer concluded by drawing attention to the value of helium for patients with a small effective lung area. A mixture of 15% cyclopropane, 20% oxygen and 65% helium gave most of the benefit of high oxygen concentration without its disadvantages, while it has been shown that there is less danger of areas of lung collapse forming distal to bronchioles plugged with secretion.

Mr. I. W. MAGILL said that in the majority of patients to whom he had given general anæsthetics for lobectomy or pneumonectomy when sputum was abundant he had tried to " get by " with endotracheal anæsthesia and intermittent endotracheal or endobronchial suction during the operation. This haphazard method was uncertain as a protection to the patient. Suction was usually applied in this manner when dislodgment of sputum from the diseased lobe was indicated by moist sounds in the trachea.

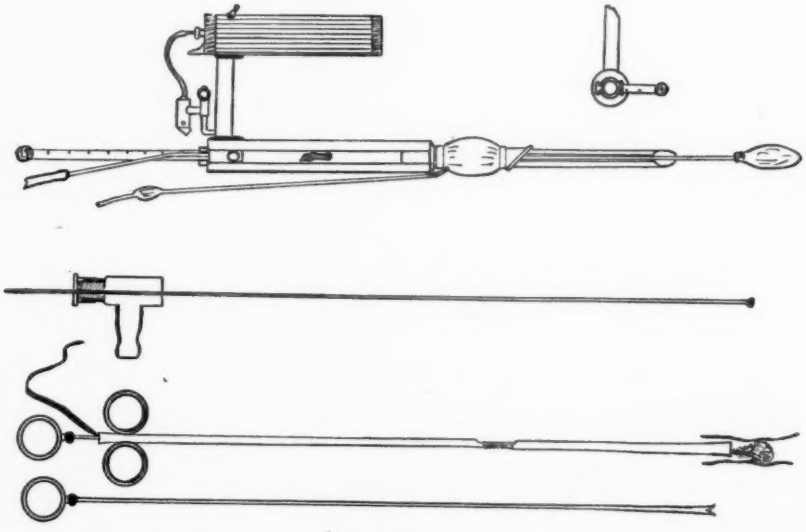

FIG. 1.

By this time, as often as not, it was too late for suction to be an effective safeguard. He referred to a combined tracheoscope and anæsthetic tube shown at a previous meeting of the Section [1]. This instrument was designed for passing into the main or secondary bronchus a suction catheter carrying an inflatable cuff, the aim being to confine secretions to the diseased area in the intervals when suction was not in progress. He still thought this method had possibilities in adult patients. A modification of the instrument was shown (fig. 1) with the addition of a Brunning type extension which enabled the introduction of an inflatable cuff to be carried out with greater accuracy. Alternatively, the instrument could be employed for bronchial tamponage (after Crafoord). For the latter purpose Allport's packing tube and plunger (illustrated) were useful. The tampon was held in position by a metal rod. Owing to a side slit the extension could be withdrawn, as well as the anæsthetic tube carrier, leaving the rod in situ.

Reference: [1] MAGILL, I. W. (1936), *Proc. Roy. Soc. Med.*, **29**, 643 (Sect. Anæs., 7).

Section of Orthopædics

President—S. L. HIGGS, F.R.C.S.

[*February* 22, 1941]

MEETING AT BOTLEYS PARK WAR HOSPITAL, CHERTSEY, SURREY

Three Patients showing the Result of Treatment of Carpal Dislocation.—F. A. SIMMONDS, F.R.C.S.

DISTRACTION apparatus has been used with success on many varieties of difficult fractures. Three cases of fracture-dislocation of the carpus have been treated by this method with sufficient success to suggest that when, for any reason, reduction by manual traction and manipulation has failed, a further attempt at reduction should be made, utilizing skeletal traction before embarking upon any open operation.

Case I.—A man, aged 34, who had a hyperextension injury to his wrist.

X-rays showed complete forward dislocation of the lunate, with rotation through 180°. Forward dislocation of the scaphoid with forward subluxation of the rest of the carpus (figs. 1 and 2).

FIG. 1.

FIG. 2.

Two attempts at manual reduction five and ten days after the accident had failed. On the tenth day he was admitted with a swollen wrist, stiff, immobile fingers and evidence of median nerve irritation. One Kirschner wire was placed through the metacarpal bases, a second through the olecranon, and screw traction applied on the Zimmer apparatus. The dislocation was reduced by manipulation whilst traction was acting, and on slackening off traction, X-rays demonstrated reduction (figs. 3 and 4).

FIG. 3.—Traction.

FIG. 4.—Traction released.

The patient was shown four months after reduction. The function of the hand and wrist was excellent. There remained some 15° loss of dorsiflexion and of palmar flexion at the wrist-joint.

Case II.—A man, aged 31, suffering from a hyperextension injury to his wrist, who had sustained a perilunar dislocation of the carpus with a fracture of the ulna styloid. Manipulative reduction had been attempted without success, five days after the injury. On admission he had the usual swollen wrist and immobile fingers with evidence of median nerve irritation. Ten days after the injury the skeletal distraction method was used, without success, thus necessitating open reduction, through a dorsal incision, when the displaced os magnum was easily shoe-horned into place.

Case III.—A man of 42, who had sustained a hyperextension injury to his wrist. X-ray showed a trans-scaphoid/perilunar dislocation of the carpus. The clinical picture was similar to that of Case II. Reduction by skeletal distraction by wires through the metacarpal bases and the radius and ulna, was attempted, without success, three weeks after the injury, and open reduction was needed.

It should have been possible to reduce the dislocation in the second patient by skeletal distraction and manipulation. It is suggested that sufficient distraction was not obtained. The third case was rendered more difficult by the fractured scaphoid, and by the fact that three weeks had elapsed before reduction was attempted. It is suggested that skeletal distraction with full aseptic technique can do no harm, and may, as in the first case, prove efficient, in the reduction of a severe carpal dislocation of some standing, and thereby obviate the need for open operation.

Moreover, in a disability of long standing, reduction at open operation may prove difficult or even impossible. We are faced with the problem of treating a dislocation which cannot be reduced.

Most surgeons are agreed that excision of the lunate alone gives a good end-result—excision of the scaphoid alone, a very poor result. If it is necessary to excise the scaphoid, the lunate should be removed at the same time, together with the cuneiform: that is, excision of the proximal row of the carpus. A fair end-result may be expected. We have patients back on full heavy work following this procedure, and with a wrist showing some 40 to 50% of the normal range. Such wrist-joints, however, are not comparable with those in which true reduction has been successfully carried out, and preferably by distraction rather than open operation.

Four Cases of Injury to the Cervical Spine.—B. H. BURNS, F.R.C.S.

Case I.—Crush fracture of the 7th cervical vertebral body, with fracture of the 6th spinous process, treated by reduction under anæsthesia and plaster fixation: subsequent relapse.

Corporal B., who was blown up at Dunkirk, had a severe crush fracture of the 7th cervical vertebral body with a fracture of the 6th spinous process, which remained undiagnosed until he saw Mr. Wiles seven weeks later. He was then admitted here.

He was complaining of pain in the neck and, at times, down the left arm. His head was held flexed and there was 50% of restriction of rotation.

Good reduction was achieved under anæsthesia by allowing the head to hyperextend. The position was maintained for fourteen weeks in a plaster incorporating the head and extending down to the iliac crest. After the plaster had been removed the deformity recurred. This, I suppose, is what we should have expected as a result of the lapse of time before the treatment was started.

His neck is still stiff and he has some pain over the site of the injury and extension is limited to 25%.

Case II.—Crush fracture of 4th and 5th cervical vertebral bodies, with flake separated from the 4th spinous process—treated by postural reduction and grafting.

L/Cpl. L. injured his neck diving into shallow water in Ireland seven months ago. He complained of pain in the neck and some pain in his arms to begin with. He was treated in a plaster collar without attempt at reduction (fig. 1).

FIG. 1 (*Case II*).—L/Cpl. L. Showing compression fracture of the 4th and 5th bodies.

FIG. 2 (*Case II*).—L/Cpl. L. Position improved and grafted.

Eleven weeks after injury he was admitted to Slough, and Mr. Hindenach was able to improve the position considerably by hyperextension in bed over sandbags. After our experience with Cpl. B. we decided to graft it straight away, a piece of tibia being placed on each side of the spinous processes. X-rays were used to check the correct levels before the final setting of the grafts.

He was in plaster for three months and has been wearing a woollen collar for one month. He now has no pain and a full range of movement except 25% restriction of flexion. Fig. 2 shows present position.

Case III.—Atlanto-axial dislocation, treated by postural reduction and prolonged recumbency.

Lt. F. was thrown from a motor cycle four months ago. Afterwards he had pain in the neck and felt he had to hold his head on, as indeed he had. It hurt him to open his mouth. Fig. 1 is the X-ray photograph.

He was put to bed with his head in hyperextension. In this position the displacement readily became reduced, and next day a radiograph showed perfect correction (fig. 2). But it was necessary to keep up the position of fairly full hyperextension or the displacement tended to recur.

FIG. 2.—Reduction in hyperextension.

FIG. 1 (*Case III*).—Lt. F. It will be seen that the anterior arch of the atlas has moved forwards so that it is now separated from odontoid process by 1/6th in.

He was placed on two mattresses, his head hanging over the upper one, with two sandbags on each side to prevent rotation. The end of the top mattress was 18 in. from the head of the bed.

To transport him here a Minerva plaster was applied and we wanted him to keep this on so that he could walk about, but, having experienced both lying fixed in bed and our plaster, he chose to lie recumbent for eight weeks. He then wore a moulded leather collar for six weeks. On removal of the collar physical treatment was started as there was considerable wasting of the cervical muscles. These soon recovered, and he is shown with a normal neck.

Case IV.—Atlanto-axial fracture dislocation; no treatment.

Mrs. D. had a bad fall two months ago, and afterwards complained of pain and restriction of movement in her neck. She was taken into a hospital in London and the X-ray showed a fracture of the odontoid process with backward displacement. At the same time she had severe bronchitis and no reduction or fixation was attempted.

She still has some pain and restriction of movement, although the pain is less and the range increasing. We have given her no treatment.

Two Cases of On-lay Bone Graft.—B. H. Burns, F.R.C.S.

Case I.—Captain D. was involved in a motor accident in France in May and sustained a compound fracture of the shafts of the radius and ulna. Amputation, advised at a French hospital, was refused.

Three weeks later the fracture was reduced here with Kirschner wires and traction and a plaster applied. At the end of August, there being no sign of union, an on-lay graft was fixed to the radius (fig. 1).

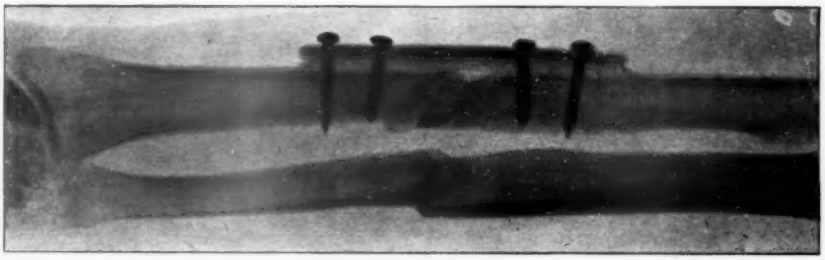

Fig. 1 (*Case I*).—Case of on-lay bone graft.

There is now union.

On-lay grafts, apparently, are much more popular in America than they are here. Henderson, of the Mayo Clinic, and Campbell, who have had great experience of ununited fractures, always use them, but they fix the graft with bone pegs; Campbell with autogenous ones, Henderson with beef bone. Vitallium screws give more certain fixation with less trouble. In my experience vitallium is as satisfactory as is claimed. The screws are inert, they cause no electrolysis and do not work loose. In a small bone like the radius, particularly, an on-lay graft has an advantage over an in-lay graft in allowing a much larger transplant and the achievement of fixation with much less skill in joinery.

Case II.—Inspector M. fractured his humerus two years ago. He was treated on conventional lines but the fracture did not unite.

A year ago he was operated on for non-union, the ends were freshened, made spike and cup shaped and impacted, no bone graft being used. I am told that it was done by a subcortical approach in order not to damage the periosteal blood supply.

Eleven and a half weeks ago a grafting operation was performed, a large piece of tibia being fixed to the humerus by six screws; the cortex was flattened by a chisel to receive the graft. This procedure has advantages over the simple freshening and impaction in securing absolute fixation and in bringing a fresh supply of osteogenetic bone to the area.

He has worn a plaster for two and a half months.

Cases shown by ROBERT YOUNG, F.R.C.S.

Mr. Young showed three cases of fractured pelvis with dislocation upwards of the sacro-iliac joint, and three cases of central dislocation of the hip-joint. The importance of early active movement and exercises was stressed particularly in those patients with central dislocation of the hip.

It was considered unnecessary to immobilize the hip-joint after reduction of a central dislocation, as the displacement showed no tendency to recur. Fixation was likely to lead to considerable stiffness of the hip. This was well illustrated by the patients shown. The youngest, a man aged 37 (Case 6), with an almost anatomical reduction of the displacement, had been immobilized in a plaster spica for six weeks. He had only a flicker of movement in the hip after a fortnight's physical treatment. At the present time he had no appreciable increase of movement after a further six weeks treatment, whereas the other two patients, one, a man aged 68, with Paget's disease affecting the injured hip, the other, a man aged 57, had an almost full range of movement in the hip and were walking well without symptoms, although there was incomplete reduction of the displacement. It was pointed out that, in view of the structural alteration at the hip-joint due to the incomplete reduction, a mechanical arthritis would probably develop later and immobilization in a spica would not prevent this. Treatment by early active movement was preferred as giving a better intermediate result than treatment by immobilization.

Two of the three cases of fractured pelvis with dislocation upwards of the sacro-iliac joint illustrated the importance of traction both in reduction of the upward displacement and in the maintenance of the corrected position. The displacement was liable to recur, and therefore traction should be maintained for a period of six weeks. During this time exercises should be carried out which would be impossible in a double spica.

CASES OF FRACTURED PELVIS WITH DISLOCATION OF THE SACRO-ILIAC JOINT

Case I.—M., aged 61. Manipulation of the pelvis in the lateral position failed to reduce the displacement although it was possible to hinge the ilium inwards. Traction with a weight of 30 lb. reduced the displacement. A double short spica was then applied; but this failed to hold reduction, and traction had to be reapplied to reduce the displacement and hold reduction.

Case II.—F., aged 44. A double short spica failed to hold reduction. Traction of 20 lb., however, easily reduced the displacement and was maintained for eight weeks. Active exercises were begun immediately after reduction, and the patient was now shown to have a full range of movement in the hip and spine and to be walking well without symptoms.

Case III.—M., aged 40. The general condition of the patient prevented any attempt at reduction for three weeks, and attempted reduction at this time failed. Active exercises were begun after removal of the plaster about a fortnight ago. The patient was shown to have about three-quarter range of movement at the hip and was walking well without symptoms.

CASES OF CENTRAL DISLOCATION OF THE HIP-JOINT

Case IV.—M., aged 57. The displacement was incompletely reduced by fourteen days' skeletal traction and he was transferred in a plaster spica. On admission this was removed and active exercises begun. No weight bearing was allowed for eight weeks. Twelve weeks after the accident the patient had almost a full range of movement at the hip and was walking well without symptoms.

Case V.—M., aged 68. This patient suffered also from transient spinal concussion as evidenced by an alteration in the visceral and somatic reflexes. The radiographs showed evidence of Paget's disease. Active exercises were begun after a week, and he had a full range of movement at the hip in about four weeks. He was up and about without weight-bearing in six weeks and was taking weight in eight weeks. He was shown to be walking well, without symptoms, and with a full range of movement at the hip.

Case VI.—M., aged 37. An almost perfect reduction had been obtained by skeletal traction for fourteen days and a plaster spica was then applied. This was removed after six weeks and active movements were begun. He still had a stiff hip with only a flicker of movement, and this was after a fortnight's physical treatment.

DISCUSSION ON INJURIES TO PERIPHERAL NERVES

Mr. Rowley Bristow: Injuries of the peripheral nerves, relatively unimportant in peace time, present a problem of the first magnitude on the occasion of a great war. Moreover the problem is many sided. First and foremost is the question of organization, and all that it entails in the treatment of patients.

Organization

Boarding and discharge.—We should keep in hospital only those patients who: (1) Are shortly to be operated upon, or (2) in whom peripheral nerve injuries are complicated by other injuries and who need further intensive remedial or rehabilitation treatment which can be carried out effectively only under in-patient conditions.

All other patients with peripheral nerve injuries, unless likely to make a quick recovery, should be invalided and discharged as soon as the injured limb has been restored to its maximal nutritional condition by physical treatment. This may occupy a period of four to nine months from the date of the wound.

Two further considerations then arise:

(1) How is continuity of *after-treatment* to be provided? This is a matter which presents no real difficulty, for the patient becomes the responsibility of the Ministry of Pensions which is in a position to arrange for appropriate treatment in an approved remedial clinic near the man's home. In actual fact in *uncomplicated peripheral nerve injuries* the need for physiotherapeutic treatment after the man has been discharged from the centre may be small, as such treatment plays no direct part in influencing recovery in the nerve. It is in those nerve injuries complicated by damage to bone and soft structures that out-patient remedial treatment is essential.

(2) A more difficult problem is arranging for the *assessment of the progress of the nerve injury* by an expert, and particularly by one who was concerned with the early investigation and treatment of the particular patient. If the special research into the subject of nerve injuries which has already been launched under the ægis of the Medical Research Council is to go forward an arrangement for follow-up is essential. It is desirable that a pensioner with a peripheral nerve injury should be re-examined at regular intervals—e.g. every two months—by an expert on the staff of one of the centres. There are two alternative methods of carrying this plan into action:

(*a*) The most convenient and efficient arrangement would be to recall the patients to the nearest centre in England, and to the similar centre in Scotland and Northern Ireland. For this it would be necessary for the Ministry of Pensions to give the scheme its backing by providing free travel warrants and subsistence when necessary. As many of these pensioners will be working, the co-operation of the Ministry of Labour will also be essential in order that employers may agree to the release of the worker for the periodical reviews.

(*b*) In exceptional circumstances a group of patients could be summoned to attend at certain times in a convenient town in a region where the neurologist would stay for two or three days, using the facilities of a local hospital for the examination sessions. In the assembly of such patients the assistance of the local orthopædic after-care clinics would, no doubt, be helpful.

The material under review in this centre at the present time is represented by 145 patients with injuries of the peripheral nerves, of which the rough analysis is shown as follows:

Ulnar	37	Ext. popliteal	12
Median	21	Int. popliteal	6
Median and ulnar ...	8	Causalgia	1
Musculospiral	27	Musculo-cutaneous ...	2
Sciatic	16		

Up to the present date we have operated on only 23 of these patients.

Pre- and post-operative treatment is on similar lines, and to be considered under two headings: (*a*) Postural. (*b*) Nutritional.

I shall only consider one or two points under these headings.

(*a*) *Relaxation of paralysed muscle.*—In the adult, even in the zero position the metacarpophalangeal joints and the interphalangeal joints will get very stiff if kept fixed. For

these joints I would advise a compromise, which is best effected by the use of the short cock-up and the musculospiral glove—this latter consists of elastic accumulators replacing the paralysed extensor tendons of the thumb and fingers.

(*b*) *We endeavour to maintain and improve nutrition,* by heat, massage, electrical stimulation, exercises and re-education. By electrical stimulation is meant interrupted galvanism to the paralysed muscle, which exhibits the so-called reaction of degeneration. I hold no strong views as to the value of electrical treatment physically, although psychically it is of great value. For a patient to see a muscle which he cannot activate voluntarily, both contract and relax, and a joint which to him is dead and useless, moved by his own muscle, must be an encouragement. Those who feel this form of treatment to be ill-advised will point out that denervation of muscle is followed after a few days by the onset of spontaneous, rhythmical contractions, fibrillation, which usher in rapid and progressive atrophy, and that to add still further to the work this degenerating muscle is forced to do is harmful.

Operative Treatment

Exact history and state.—Whilst it is true that in the treatment of a patient with an injured peripheral nerve operation is only one part of treatment, yet it is an important part. Before operating the surgeon must have previous knowledge of the patient's story and an exact estimate of his disability. If the lesion is complete anatomical division, with an end bulb, it may not matter, but with an incomplete lesion, or a fusiform neuroma, with the nerve in anatomical continuity it is vital that the surgeon must know just how far he is prepared to go, how far it is wise to resect and sacrifice some conducting fibres.

Again no operation should take place unless the surgeon is prepared to test the electrical reaction of the exposed nerve, either with a faradic coil or with a condenser discharge apparatus. This procedure has a use other than that of merely testing conduction. It may and does assist in deciding on the identification of an intact nerve, in regions where the anatomy may be difficult and relations altered by scarring and by old fractures, by displacement and matting of soft parts, and this is particularly true in the exploration of nerves wounded in the axilla.

Time for operation.—It has been laid down by the Medical Research Council that, so far as is known, there is no lapse of time, between division of a nerve and its suture, which precludes recovery. Stopford, writing in the *British Journal of Surgery* in 1922, states that re-suture may succeed up to three years from the time of the injury. Stiles, writing in Robert Jones's "Othopædic Surgery of Injuries", advocates early operation, as the result of his big experience of nerve suture at the Bangour Hospital, Edinburgh. Most surgeons advise that operation should not be delayed unduly, always provided that all wounds have been healed for a period sufficiently long to render the chance of a recrudescence of sepsis unlikely. There is the further point that joint stiffness should be overcome as a preliminary, as it may be necessary to alter the posture of certain joints in order to approximate divided nerve ends during the actual operation.

Operation may be considered under four headings : (1) End-to-end suture. (2) Neurolysis. (3) Bridge operations (nerve grafting). (4) Operation to improve function, in irreparable injuries.

(1) End-to-End Suture

To effect end-to-end suture is the main object and the only satisfactory method of restoring conductivity in a divided nerve.

It is necessary to find the nerve above and below the site of injury and not to search for it in dense scar tissue. The nerve may be freely mobilized, and it is on mobilization rather than stretching that one relies for overcoming the gap. It has been suggested that there is a fear of ischæmia if the nerve sheath is stripped over too great a length. I have often seen the ulnar stripped from the axilla to the wrist, with no ill-effect. The nerve can be stretched, in addition, but this gives no great increase in length.

Alteration of posture, by flexion of the wrist, adduction of the arm and so forth, will help to overcome a gap. In operating on the sciatic nerve or either of its two main divisions, one should remember that, in addition to flexing the knee, extension of the hip is of great value.

If advantage has been taken of change of posture to approximate nerve ends, the patient

leaves the theatre with the appropriate splintage to hold this posture. The position should be changed gradually. The limb should be kept splinted in the original position for a minimum period of three weeks, ensuring relaxation of the sutured nerve, and then, over the next three to four weeks, nearly eight weeks in all, it is gradually freed. Any sudden or too early stretching may cause disaster in that the suture line may give way.

Mobilization of the nerve by stripping up of motor branches will make for ease in closing a gap. This procedure is most often called for in transposition of the ulnar to the front of the elbow. *Transposition* of this nerve is frequently necessary. More rarely the musculospiral may be transposed with advantage to the front of the humerus, resulting in a gain in length of an inch to an inch and a half.

Finally, to obtain end-to-end suture, the so-called *two-stage* operation is sometimes called for, usually with a lesion of the median or sciatic. If on exposure it is obvious that, with resection of the end bulbs, the gap will prove too wide for the nerve ends to be approximated, the nerve is mobilized, every advantage taken of altering posture and the two end bulbs are joined by stout thread or strong catgut, under some tension. Over the next two to three weeks the posture is gradually altered and then the nerve is re-explored, when successful suture may be possible.

Bone shortening is generally only undertaken if the nerve injury is combined with a fracture, and, although somewhat lightly recommended at times, is a formidable undertaking, at least for the patient. It is worth considering with an otherwise inoperable lesion of the median, as the disability following complete sensory loss in this nerve is crippling.

Technique of suture.—There are a few points worthy of notice and discussion. The best material for suture is 160 linen thread as recommended and used by Stiles, and the sheath only is sutured. It was shown by Sargent and Greenfield that the fineness of the suture material was the important factor, and for this reason 0000 catgut was given up, and as a routine, fine white silk or, better, Stiles's 160 linen thread should be used as the suture material. The amount of nerve to be resected sometimes presents a difficulty. Following sepsis there may be a considerable degree of intraneural fibrosis, and the surgeon may be doubtful how much nerve he must resect. The mobility of the sheath is a useful guide. If the sheath peels back, the pairing is probably sufficient. Experience only can help one to decide how much should be sacrificed and how far one can go without jeopardizing the chance of end-to-end suture. No wrapping by fat, fascia or Cargile membrane was found to be of value. In nerves which had been wrapped and were re-explored, the reaction and fibrous tissue which had formed was always found to be excessive. This was particularly so if Cargile membrane had been used, and this was discarded early as the result of our experience. A good clean bed for the nerve should be provided as far as possible and the nerve must be freed from tendon if it is adherent, as is often the case with a lesion of the median in the forearm. The experimental work at Oxford, in the use of the fibrinogen plasma "glue" will be watched with great interest. Anything which will lessen the fibrosis occurring at the line of junction must be helpful, but it is so often necessary to suture with some degree of tension that it seems likely that stitching of the sheath will be needed in the majority of suture operations. The use of "glue" in fixing autogenous cable grafts may prove of value, and it is to be hoped that a simpler preparation will be found and standardized for this purpose of joining nerve ends.

(2) Neurolysis

The main use of this operation lies in the freeing of the nerve from scar, and so restoring its mobility, rather than in relieving compression. It is difficult to assess the value of the operation, and statistical survey of the results of neurolysis appears to me useless. Long-continued compression or irritation leads to interstitial neuritis. Once this has occurred, neurolysis or alteration of the nerve bed by transposition may prevent the change from progressing, but there is not much evidence of recovery. For example, transposition of the ulnar for delayed involvement following an old fracture of the external condyle, is not followed by any great increase in bulk of the ulnar intrinsic muscles The operation is of value to prevent progressive wasting. Neurolysis should be regarded as an exploratory operation and is often the first line of attack against pain, and even against the rare and distressing syndrome, causalgia. The freeing of the nerve from scar and placing in a new bed often relieves pain. For true causalgia, resection and suture may even be called for. I fail to see the rationale of slicing the nerve sheath for an intraneural fibroma, with a

nerve in anatomical continuity; but a damaged and thickened sheath, adherent to a scarred nerve bed, should be removed.

(3) Bridge Operations

These include *neuroplasty*, the turning down of flaps from the intact nerve above, and *tubulization*, that is joining the divided ends by a tunnel made of vein, fascia or membrane. These two methods will always fail, and should not be practised.

Nerve grafts were tried by many surgeons, in this country, in America and on the Continent. The British and American surgeons condemned them almost unanimously. It may be said that, in the main, grafting operations failed in the treatment of nerve injuries in the War (1914-18). Some few patients in whom the operator claimed some degree of success were examined by a Committee of the Medical Research Council. It is true that two or three patients examined showed evidence of growth of axons through the graft and of voluntary action in muscles supplied by the nerve below the point of division. No single patient showed any real recovery of function, either sensory or motor. All types of graft were employed, and it was generally agreed that autogenous cable grafts offered the best hope of success. Joyce, of Reading, in a contribution to the *British Journal of Surgery* (1919, 6, 418) showed evidence of slight regeneration following grafting. In the main, few new axons appear to get through, and the degree of crossing and shunting which takes place is well shown in Dr. Greenfield's sections. Later work on the facial nerve has shown some interesting results, and evidence of successful grafting is established. It may be that, with improved technique and by the use of "glue", the results will improve. In my opinion, grafting is a method which should be employed only if all efforts to obtain end-to-end suture, even by the two-stage operation, are a failure. Then an autogenous cable graft should be used. The value or otherwise of grafting can be tried out and will be tried out on the human subject which is the point at issue. That grafting succeeds in rabbits and monkeys is well known; that it succeeds in the nerves in the limbs in man is unproved at present.

(4) Operation to Improve Function

When there is no recovery of conduction in the nerve.

The few points I would remind you of are best considered under individual nerves:

(*a*) *Sciatic.*—Two avoidable consequences, viz. the short tendo Achillis, with fixed equinus of foot, and the fixed flexion contracture of the interphalangeal joint of the great toe should be remembered and guarded against. The thin, useless and often painful foot following a lesion of the sciatic nerve when there is incomplete recovery or no recovery, is best treated by amputation below the knee.

(*b*) *External popliteal.*—The loss of dorsiflexion is better treated by one of the many forms of toe-raising spring, or similar appliances, than by operation. Tenodesis, the fixing of the paralysed tendons into the tibia and so making a new ligament, failed in practice because the tendons stretched and the drop-foot reappeared.

(*c*) *Median.*—It is the sensory loss which is the disability, and the uselessness of the thumb and index which thereby ensues. Nothing can be done, in the absence of at least partial recovery in conduction of the nerve.

(*d*) *Ulnar.*—Again, as in the median, no alternative treatment is of value, but here it may be stated that an ulnar lesion is not necessarily a crippling disability. It all depends on the man's work. I have already reported the case of a man who earned his living as a bricklayer who had a complete ulnar lesion of eighteen years' standing.

(*e*) *Musculospiral.*—Here tendon transplantation is of real value. The standard operation is shown in the patient before you. Briefly, pronator radii teres is transplanted into extensor carpi radialis longior and brevior, flexor carpi ulnaris into extensor communis digitorum and extensor longus pollicis, and flexor carpi radialis into extensor ossis metacarpi and brevis pollicis. This operation gives a good functional result and a useful hand, which a working man can use. It should be employed without hesitation, following a musculospiral lesion, when end-to-end suture is impossible. It should be used also in my judgment for posterior interosseus injury. Platt has had success with the suture of this latter nerve, but, depending on the exact site of the lesion, tendon transplantation offers a good alternative.

Results

Pathological reasons for failure.—There are many reasons for the poor success which resulted from our efforts. Apart altogether from avoidable sources of failure, e.g. operation sepsis, there are definite pathological changes in the nerve in war wounds complicated, as they usually are, by major or minor sepsis at the time. These changes will be demonstrated by Professor Greenfield in the slides which were made from sections which he prepared for us. Platt and I reported on the *Diagnosis and Treatment of Peripheral Nerve Injuries* for the Medical Research Council in 1920. They may be classified as:

Changes above point of suture. (*a*) Interstitial fibrosis sometimes extending 8 in. or more up the nerve. (*b*) Ascending toxic neuritis. (*c*) Degeneration of cells of the anterior horn or root ganglion.

Changes about the line of suture. (a) Fibrosis round the stitch. (*b*) Bad shunting (Stopford). (*c*) Alteration of the intraneural anatomy. This cause of failure is well exemplified in the figures in Young's article in the *Lancet*, 1940, (ii) 126.

Changes below the line of suture. (*a*) Failure of myelination. (*b*) Incomplete regeneration. This process may have gone on normally for a time and then for some reason finished and no further regeneration occurs.

Tables of results following on the Great War are published, and there is no object in repeating these lists. The interest lies in the results of end-to-end suture and of grafting operations. These latter I have already referred to. The results of suture were summarized by Stopford of Manchester, who together with Platt has published the most complete figures, as follows: "Imperfect recovery of function and sensation is almost invariably found under the most favourable circumstances after secondary suture and resuture." The figures vary with the observer, and this is particularly so in studying the results of neurolysis operations. As already stated, this operation should be regarded often as exploratory, and it is likely that it has had no effect on the end-result. Among the results of suture, as is well known, the musculospiral heads the list of recoveries, but even with this nerve, the synergic action of the wrist extensors is often lacking. The results of suture of the *ulnar* are physiologically poor, economically or functionally good. If the sensation to pin-prink is restored, even with poor intrinsic muscles, the hand can be strong and useful. The finer movements needed for such action as piano playing or delicate work will not be regained. The *median* results are on the whole poor because of failure of recovery in sensation in the thumb and index. Recovery of sensation will be incomplete, but recovery of appreciation of pin-prick will safeguard the patient against injury. The finer forms of discrimination are unlikely to be regained in full. The *sciatic* results are on the whole poor. In my experience, recovery of motor power is usual in the calf, though likely to be incomplete in the external popliteal element; but far more serious is the loss of sensation in the sole and the wasting of the foot. Even without definite trophic change, the thin wasted foot is very liable to injury and, if sensation is permanently and badly impaired, amputation will be called for.

The picture of recovery then, as I know it, is not very encouraging, but it depends in part on what our criterion of recovery is. Is it neurological or is it recovery of gross function? Farquhar Buzzard, writing in Jones's "Orthopædic Surgery of Injuries", says:

> "Speaking generally it may be said that injuries to nerves, even when they involve complete division may under favourable circumstances be successfully treated in so far as a certain degree of usefulness is restored to a limb, but that if the parts involved are needed for highly specialized movements or for sustained effort, they are almost certain to be found wanting."

Dr. J. StC. Elkington: In 1941 we resume the study of a problem which has been as it were in cold storage for twenty years and is substantially the same as it was in 1920.

From the clinical point of view lesions of the peripheral nerves constitute a number of clear-cut and uniform pictures. This is to be expected as they are relatively simple structures with fairly constant anatomical and very constant physiological properties.

The great majority of peripheral nerves contain fibres of three types:

(1) *Somatic efferent fibres* carrying impulses from the anterior horn cells to the voluntary muscles.

(2) *Autonomic efferent fibres* carrying impulses from the sympathetic centres to innervate the blood-vessels, sweat glands and smooth muscles.

(3) *Afferent fibres* carrying impulses from the sensory organs in the skin and deep structures to the spinal cord.

In consequence in any peripheral nerve lesion, disturbances of function are likely to be found in respect of: (1) Motor function; (2) Autonomic function; (3) Sensory function.

(1) Motor function: The muscles supplied by the injured nerve manifest the usual signs of a lower motor neurone lesion, namely, atonia, wasting, loss of voluntary movement and changes in electrical reaction. This loss of power may often to some extent be masked by the development of " trick movements ". On the other hand precisely similar changes may result from injury to the nerve which does not involve actual anatomical severance, and distinction between physiological and anatomical interruption of a nerve may be impossible except by inspection. Cases are not uncommon where the motor function of a nerve is temporarily lost while its sensory function remains normal.

(2) Autonomic function: Changes in the skin and tissues, probably the result of interference in the autonomic innervation, comprise loss of sweating, thinning of the skin, atrophy of the tips of the digits, changes in the nails, hypertrichosis, osteoporosis and reduced power of healing. A number of problems in connexion with the autonomic function of peripheral nerves suggest themselves, for example the rate of regeneration of the fibres, the nature of the so-called trophic disturbances and their possible connexion with spontaneous pain.

(3) Sensory function: In lesions of peripheral nerves sensory function may be disturbed in one of two ways. There may be diminution or loss of one or more varieties of sensation and there may be spontaneous sensation in the absence of any adequate stimulus, taking the form of spontaneous pain, paræsthesia and hyperæsthesia.

Sensory loss: The great majority of peripheral nerves contain afferent fibres carrying impulses from the skin and deeper structures, and interruption of these fibres gives rise to a greater or lesser degree of sensory loss. The estimation of this sensory loss, particularly as regards the different modalities of cutaneous sensation, constitutes one of the most important and at the same time quite the most difficult part of the examination of these cases.

Sensation may be usefully divided into two orders: (1) Superficial sensation consisting of sensibility to pain, temperature and light touch; (2) deep sensation consisting of sense of position and passive movement and of deep pressure.

It will be found that the area of complete sensory loss is invariably much less than the whole area innervated by the nerve on account of the overlap from contiguous nerve fields. Indeed in many cases, such as the musculospiral or musculocutaneous nerves, there is no area of complete anæsthesia at all. But in the case of such nerves as the median and ulnar there will be found a relatively small area where there is complete loss of all forms of cutaneous sensation as well as of deep pressure. This is the so-called area of exclusive supply of that nerve. Over the remainder of the area anatomically supplied by the nerve it will usually be found that cutaneous sensation is present but is modified in character. Pain—high threshold, delay, radiation, emotion. Touch—absent. Temperature—discrimination lost between 22° and 40°. Compass point discrimination lost. Over this area deep pressure is preserved. This modified type of sensation was termed by Head " protopathic sensibility " as opposed to normal sensation of a highly discriminative type which he termed " epicritic ". These names, while having a useful function as descriptive terms, have unfortunately become so much involved in an elaborate theory of nervous function for which the evidence is, to say the least of it, far from convincing, that their retention is on the whole prejudicial to careful examination and to clear thinking. During the recovery of sensory function after regeneration of a sensory nerve, the first step is usually the return of crude forms of sensation to the previously anæsthetic area, followed by a gradual shrinkage from without inwards of the abnormal area until a state of stability is reached which unfortunately usually falls short of normal function. The explanation of the constancy of the features in partially denervated areas of skin remains a subject for speculation.

For the examination of the sensitivity of the skin various methods are available. A pin, a wisp of cotton-wool and hot and cold test tubes are employed to test sensibility to pain, touch and temperature respectively. There are also instruments of greater precision; æsthesiometers of different types, Von Frey's hairs, tubes of graduated temperature. However, the use of accurate instruments does not guarantee accurate results. All sensory examination involves two very important subjective variables—the examinee and the

examiner. The patient should be warm and comfortable and quiet. He should have a feeling of confidence in the examiner and should understand what he is doing and why he is doing it. Probably half an hour of examination at a session is as long as the average patient can stand. The same conditions in general apply to the examiner.

In addition to sensory impairment or loss, the area affected by a peripheral nerve lesion may be the site of *abnormal spontaneous sensations*. These may take the form of hyperæsthesia, tingling, pins and needles and *pain*. The latter varies greatly in intensity from a slight discomfort to the excruciating agony which forms the essential feature of *causalgia*. The difference to me seems essentially one of degree rather than of kind. The pain of causalgia is described as a constant burning discomfort which is greatly accentuated by contact, noise, fatigue and many emotional factors, especially of an unpleasant character. The pain is sufficient to exert a most serious effect upon the individual's general health and character. The affected part shows to a marked degree the "trophic disturbances" seen in peripheral nerve lesions. The condition is especially liable to occur in lesions of the median and sciatic nerves when the nerves have been involved in areas of infection or submitted to severe contusion.

Dr. J. G. Greenfield showed some lantern slides illustrating the microscopical appearances of injuries to nerves. He pointed out that unsatisfactory results after end-to-end suture or nerve grafting might result from unhealthy conditions of the nerve above, at, or below the level of suture. *Above the level of suture* the most usual abnormality was thickening of the endoneurium of the nerve, which might be associated with œdema. This appeared to result from upward travel of toxins arising from septic infection of the nerve. In one case of long-continued sepsis of the ankle-joint, for which the leg had to be amputated below the knee, examination of the posterior tibial nerve 8 in. above the ankle showed extensive fibrosis of all the sheaths of the nerve; many bundles had become completely, and others partially, demyelinated and sclerosed.

At the level of injury the character of the scar tissue had a definite influence on the outcome of the operation. If sepsis, or any irritating foreign body such as catgut or even silk sutures were present to cause excessive connective tissue overgrowth, the neuroma joining the upper and lower ends of the nerve was likely to be poorly innervated, or the nerve fibres penetrating it might be killed later by the contraction of the newly formed connective tissue. He showed slides of a specimen of unsatisfactory nerve graft, in which a silk suture through the upper cut end of the nerve had caused severe fibrosis and small-celled infiltration, which must have obstructed the outgrowth of new nerve fibres to a considerable degree.

In the lower end, so long as the tissues were properly nourished, the nerve, after undergoing Wallerian degeneration, remained ready to receive new axis cylinders and to conduct them to the nerve endings. It was rare for nerve fibres to be impeded in their regeneration once they had bridged the neuroma at the junction and entered the peripheral cut end of the nerve. In a case of gunshot wound dividing both the sciatic nerve and the femoral artery, published by Platt and Bristow, things had not gone forward in this manner: following end-to-end suture of the sciatic nerve there was some recovery of power and sensibility, but the foot remained for many months in a condition in which every stimulus gave rise to diffuse unpleasant tingling, as in the stage of recovery which was named "protopathic" by Sir Henry Head. The condition was so intolerable to the patient that the leg had to be amputated below the knee. Examination of the nerves near the level of amputation showed that new axones had passed in profusion into both the internal and external popliteal divisions of the nerve, but almost all of them had remained unmyelinated. It was tempting to attribute the partial nature of the regeneration in these nerves to inadequate blood supply.

Mr. Jocelyn Swan said that he looked upon preoperative treatment as most important, and he was strongly in favour of galvanic stimulation of paralysed muscles in order to keep up the general tone and nutrition of a paralysed limb. He did not agree with those who said that galvanic stimulation overtired the muscle, but he thought that, with proper splinting to prevent over-stretching of the muscle and with galvanic response, a great deal could be done. He was of opinion that no operation should be performed on a presumed nerve injury until a full four to five months had elapsed from the time of the wound, and then only provided that the wound had been completely healed for fully three months, was soft and supple and that the general nutrition of the limb had been maintained by

physiotherapy. In judging the necessity for operation, he relied largely on the condenser discharge tests of paralysed muscles, and if, in successive examinations, the muscles responded to a smaller condenser current there was a strong probability of muscle recovery without operation. He agreed most decidedly with Mr. Bristow as to the great advantage of a wide exposure of the nerve, exposing it freely both above and below the injured area before dealing with the scarred portion. Direct stimulation of the nerve by weak bipolar faradic current should always be undertaken. Although he condemned most thoroughly all attempts at bridging an interval between the nerve ends or at tubulization between them, he said it was occasionally necessary to fill the gap by means of an autogenous nerve graft. He carried this out on eleven occasions and in three cases success was obtained, but with greater experience and with the wide exposure advocated by Mr. Bristow, nerve grafting would become less frequent. Often there were serious complicating injuries, notably to the bones and the vascular supply of the limb. He felt that serious bony disabilities, such as malunited or ununited fracture, should be dealt with before the nerve.

It was difficult to speak of results as so many of the cases which were operated upon were transferred to other hospitals and could not be followed up. He had been able to follow a large number for two or three years and he agreed with Mr. Bristow that the best results were obtained after operations on the musculospiral nerve, and that both the median and the sciatic nerve gave poor results. He did not agree that the results of the external popliteal nerve injuries were poor and was inclined to place these only second to the musculospiral; neither did he agree that operations on the posterior interosseous nerve were doomed to failure, as he had had more than one which gave fair results after surgical attack. In many of these cases, however, he would prefer to do a tendon transplantation in the forearm which had yielded good results.

[*See also* page 521, Section of Surgery.]

Section of Surgery

President—J. B. HUNTER, M.C., M.Ch.

[*April* 2, 1941]

DISCUSSION ON INJURIES TO THE PERIPHERAL NERVES

Mr. Jocelyn Swan: During war-time, lesions of the peripheral nerves form a fairly large proportion of total casualties. In a statistical report which Dr. Worster-Drought drew up in November 1921 and which was published in the *Journal of the Royal Army Medical Corps*, he tabulated no less than 1,944 peripheral nerve injuries in a total number of 1,602 patients, and it is of some interest to analyse these according to the frequency with which individual nerves were affected.

Included in this total there were 114 cases of injury to the brachial plexus and this naturally included a number of multiple injuries. Thus, in 83 cases in which the cords alone of the plexus were injured, there were lesions to 115 cords. Of the remaining part of the upper limb, in 799 cases there were 250 instances of lesions of the musculospiral nerve, 323 of the median and 330 of the ulnar; so that our figures do not bring out the relatively large proportion of ulnar nerve injuries that are quoted by many authors. It is interesting to note, however, that in no less than 84 cases, the median and ulnar nerves had suffered injury by the same wound. Of the 546 injuries to the nerves of the lower limb, there were 189 cases of injury to the trunk of the sciatic nerve, whilst there were 162 of the external popliteal and 76 of the internal popliteal nerve. There were also 64 cases of injury to the posterior tibial nerve.

TABLE I.

Brachial plexus

Roots of brachial plexus	Alone	31	
Outer cord	Total	23	8
Posterior cord	,,	53	34
Inner cord	,,	39	18
Outer and posterior cords	..	..	2
Outer and inner cords	..	..	4
Posterior and inner cords	..	..	8
Outer, posterior and inner cords	..	..	9
Total cases of brachial plexus injury, 114		115	114

The type of injury suffered by a peripheral nerve in warfare roughly falls into two groups: the first where there is a temporary loss of conduction without actual macroscopic injury to the nerve trunk, which is occasioned by the passage of a bullet of high velocity in the immediate vicinity of the nerve causing a physiological block. There is no disruption of the sheath of the nerve and there may be no actual degeneration of the axis cylinders. There is comparatively little muscle wasting and recovery usually takes place in a few weeks under adequate treatment. The other large group consists of cases in which there is a loss of conduction in the nerve due either to complete section or to an injury which

TABLE II.

Other nerves of the upper limb

Musculospiral	Total	250	Alone	199
Median	,,	323	,,	173
Ulnar	,,	330	,,	205
Musculo-cutaneous	,,	24	,,	1
Circumflex	,,	4	,,	4
Internal cutaneous	,,	49	,,	10
Lesser internal cutaneous	,,	2	,,	—
Posterior interosseous	,,	22	,,	15
Radial	,,	9	,,	—
Anterior interosseous	,,	1	,,	1
Multiple :				
Musculospiral and median				26
,, ,, ulnar				12
,, ,, musculo-cutaneous				6
,, ,, internal cutaneous				2
Median and ulnar				84
,, ,, musculo-cutaneous				6
,, ,, posterior interosseous				1
Ulnar and internal cutaneous				16
,, ,, posterior interosseous				2
Posterior interosseous and radial				1
Median and radial				4
Musculo-cutaneous (branch of) and radial				1
Internal cutaneous and lesser internal cutaneous				1
Musculospiral, median and ulnar				2
Median, ulnar, and musculo-cutaneous				2
,, ,, ,, internal cutaneous				12
,, posterior interosseous and radial				2
,, ulnar, and posterior interosseous				1
,, ,, ,, lesser internal cutaneous				1
Musculospiral, median, ulnar, and internal cutaneous				2
,, ,, ,, ,, musculo-cutaneous				1
Median, ulnar, musculo-cutaneous and internal cutaneous				6
	Total cases			799

TABLE III.

Other nerves of the lower limb

Sciatic (trunk)	Total	189	Alone	184
Small sciatic	,,	15	,,	10
External popliteal	,,	162	,,	126
Internal ,,	,,	76	,,	42
Musculo-cutaneous	,,	29	,,	26
Anterior tibial	,,	13	,,	10
Posterior ,,	,,	64	,,	56
Anterior crural	,,	14	,,	12
External cutaneous	,,	4	,,	3
Middle ,,	,,	6	,,	6
Internal ,,	,,	5	,,	4
,, saphenous	,,	12	,,	6
Obturator	,,	2	,,	1
External saphenous	,,	4	,,	2
Plantar	,,	2	,,	2
Multiple :				
Sciatic and small sciatic				5
External popliteal and internal popliteal				34
,, ,, ,, external saphenous				2
Anterior crural and external cutaneous				1
,, ,, ,, obturator				1
Internal cutaneous and internal saphenous				1
Posterior tibial and internal saphenous				2
,, ,, ,, anterior tibial				2
,, ,, ,, musculo-cutaneous				3
,, ,, anterior tibial and internal saphenous				3
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has opened the perineural sheath and caused partial damage to the trunk of the nerve to a greater or less extent.

As opposed to the cases which are seen *in civil life* and which are mainly of complete severance of a nerve trunk or to the block of impulses to compression of the nerve, we have to consider *in war injuries the influence of sepsis* which occurs in the wound and the effect not only to the surrounding structures but to the nerve itself. Infection of the wound, which may be of some weeks' standing, leads not only to destruction of the tissues, but to the formation of a large amount of fibrous tissue in the immediate vicinity of the nerve injury. It also leads to the formation of intraneural fibrosis extending principally in the proximal end of the nerve and interfering with the formation of new axis cylinders. This intraneural fibrosis forms an enormously important factor in dealing with these war injuries and should always be in the surgeon's mind when he is considering whether he should resect a given injury or be content with separating the nerve out from the scar tissue. Formation of fibrous tissue in the immediate vicinity of the wound prevents the delicate axis cylinders from finding their way to the neurilemmal sheaths in the distal end. It is only fair to say that it can only rarely be shown by operation that the block in the nerve conduction is entirely due to pressure from outside. It has been my experience, however, to operate on cases in which I have found this compression of the scar tissue to be the cause of the physiological block in nerve conduction, and that the relief of compression has been followed by recovery at a quicker rate than is usual. In the large majority of cases *there has been a primary injury to the nerve* and, though at operation there may not be complete division of the nerve, the symptoms show that there is a complete block even in the part which looks intact, and I feel that this particular block is due to intraneural fibrosis in that portion and that perineural fibrosis only plays a secondary part. It is interesting to note that in one case Professor Stopford found intraneural fibrosis to extend as far as 8 in. up the proximal end of the nerve.

In testing the motor functions of an individual muscle one must be sure that the movement one is trying to elicit is not done by some trick movement of an entirely different muscle; as for instance when flexion of the wrist is produced by the long abductor of the thumb, or when flexion of the fingers is caused by dorsi-extension of the wrist. There are, too, occasional instances in which a particular muscle may have an irregular nerve supply; I have seen the first dorsal interosseous muscle supplied by the median, and the flexor carpi ulnaris muscle to be in full action when there has been a complete severance of the ulnar nerve in the arm. Some reliance may be placed on faradic reactions of paralysed muscles, but I do not trust to the so-called reaction of degeneration in galvanic tests. At Woolwich we placed considerable reliance upon the condenser reactions. *Regular periodic examination* of every patient should be made before any operative procedure, as it is only by observing the changes which take place in the function of the limb at successive examinations that an opinion can be given as to operation or further general treatment. No case, except in the special emergency of causalgia, should be operated upon until at least a period of five months has elapsed from the date of the injury, and then only provided that the wound has been soundly healed and has shown a soft supple scar for a period of two months. During this time general physiotherapeutic treatment should be carried out for the injured limb in order to maintain the nutrition of the muscles and the mobility of the distal joints. The paralysed muscles should be kept in relaxation by efficient postural methods. The limb should be kept warm and have daily massage, passive movements and electrical stimulation and exercises. My own aim is to keep the paralysed muscles stimulated by galvanic response, and it is of particular importance in the upper limb to retain the movements of the fingers and thumb, and for this reason no splints should extend beyond the heads of the metacarpal bones. At the same time, the patient should be taught to take an intelligent interest in what is being done for him, as the results of these nerve injuries depend very largely on obtaining his active co-operation and interest. He should understand that any operation which is contemplated is merely an incident in his treatment which will have to be carried on for several months after the operation has taken place. When *recovery is commencing* either with or without an operation, the first sign is usually a change in the vasomotor effect. The skin of the peripheral supply of the nerve which had become thin, glossy and dry becomes more normal, whilst the sensory areas in which either painful or light touch were not present may become hyperæsthetic. Pressure sense returns early. The patient says that he feels that something different is taking place in the limb, usually that he feels " more life in

it ", and there is a gradual progressive decrease in the area of anæsthesia commencing in the proximal part. The muscles supplied by the nerve may become tender on pressure and after a time commencing voluntary action may be observed in the proximal muscles and a response to strong faradic current may be elicited. In some cases voluntary movement may be seen before any faradic response is obtained, but this is a variable quantity. A much more certain method of testing is by the condenser reactions when the muscles will be found to contract to a stop two or even three times smaller than occurred on a previous occasion. I do not place much reliance upon *Tinel's sign,* that is the feeling of formication in the sensory distribution of the nerve on percussion along its anatomical course.

A new nerve axis cylinder is said to grow at the rate of about one inch in twenty-five days and, although Tinel's sign may show that some regeneration of nerve axons into the distal segment has taken place, it does not necessarily follow that sensory fibres have found their way into the sensory channels, rather they may have passed into motor channels becoming ultimately connected to motor end-plates which can have no action in producing contraction of the muscle. The presence of formication in the distal distribution again does not give any indication of the bulk of nerve which has regenerated, and if the sign is to be relied upon it should be progressive along the course of the nerve in the periodic monthly examinations.

What then are the *indications which would lead the neurologist to advise operation* in a case of injury to a peripheral nerve? The first obvious indication for operation is the *persistence of complete paralysis* of the muscles supplied by the nerve with no change in the sensory distribution nor of the faradic reactions of the muscle, and which do not respond to a condenser test to a smaller stop than a No. 10 in the periodic examinations which have been carried out. I place a limit of five months between the time of the injury and any operative interference because it is during that time one would have expected signs of recovery to have occurred if regeneration is taking place; and, though it would seem that early operations should give a more favourable result, it has been shown by Professor Stopford that recovery in the nerve may take place even after an interval as long as two years from the time of primary injury. The *palpation of a thickened* mass in the part of the nerve at the site of injury would also be an indication for operation as this usually means that a complete section of the nerve has occurred and the thickened palpable mass is the bulbous enlargement of the proximal end. I would also advise operation in a case in which *early recovery* had been noted but *which had not progressed;* or again, if these early signs of recovery have retrogressed; and possibly in some cases I would advise a reoperation if there had been no sign of recovery after a period of twelve to eighteen months from the previous operation on the nerve. Secondary operations on nerve trunks may be required owing to faulty technique which has been adopted, and in one case under my care I found a nerve had been sutured to a distal tendon. Cases occur in which a good deal of difficulty may arise as to the necessity for operation, when a certain amount of recovery has occurred in the proximal muscles but the distal paralysis and disturbances of sensation remain complete. Is this a condition in which partial recovery has taken place but has not progressed, or is it one in which one may expect no further improvement to occur? This condition has been aptly described by Mr. Harry Platt as the " syndrome of incomplete conduction " and it may occur when there is no complete severance of the nerve, but in the fusiform spindle swelling which is occasionally seen at the seat of injury. I would again emphasize the necessity of active physiotherapeutic treatment before operation is undertaken as I feel it is not of the slightest use operating upon cases of nerve injury where the muscles have been allowed to become fibrotic, the fingers fixed by fibrosis in the interphalangeal joints, or where extensive contractures have taken place from the loss of muscle substance. Most of these are preventable by adequate treatment, early mobilization and by re-education methods, and it will be interesting to see during the progress of this war whether the methods of treatment by closed plaster, sulphanilamide and skin grafting may bring the tissues into better condition, and that these muscle changes may be prevented. The immediate suture of a divided nerve at the primary debridement operation were all failures in the last war.

Operative technique.—Due thought must be given to the *position of the limb* at the time of the operation and more particularly to the position which may have to be maintained after the operation has been completed; I make it a rule always to have a cast made

of the limb in the position which I think it will have to be maintained afterwards, and be ready to apply it at the end of the operation. For instance, if I am going to operate on the trunk of a sciatic nerve where I think that flexion of the knee-joint will be necessary to bring the two ends of the nerve together, I have a mould made to fix the knee in the flexed position which can be applied directly the operation is completed. With a fairly extensive experience of operating upon these nerve cases, one learned the necessity of *a wide exposure of the nerve trunk* both above and below the injury. The nerve should be exposed in its anatomical position, preferably in an intermuscular plane, above and below the injury before any attempt is made to free it from the extensive fibrosis which has occurred from the concurrent sepsis. It is necessary in some cases to expose the nerve for several inches, stripping up any muscular branches which may be exposed in order better to approximate the ends of the nerve should resection be demanded. At the stage when the nerve has been exposed above and below the injury, direct faradic stimulation of it should be made with the minimal current and observation made for any contraction in the muscles supplied by the nerve. This method was first adopted by Mr. Rowley Bristow. For this stimulation I prefer a bipolar method to diminish the effects of diffusion of the current by two fine electrodes placed close together. In our earlier work with this method we hoped to learn something about the actual topography of the nerve fibres, but I am afraid this did not lead us very far. One thing we did learn, however, with this direct stimulation was that we were more easily able to identify nerves where one was dealing with such a situation as matting of the cords of the brachial plexus. If there is complete section of the nerve, no reaction will be obtained by stimulation above it, but occasionally direct stimulation above a lesion will show that there is a certain amount of conduction in the nerve, whilst a reaction in the distal part will show at all events that some nerve fibres are present which are capable of excitation. In the majority of cases, however, even where the lesion does not prove to be a complete section of the nerve, excessive intraneural fibrosis will prevent any conduction through it.

It is *only after free exposure above and below* the lesion that the nerve should be followed through the dense cicatricial tissue in the immediate area of injury, when a wide variety of conditions may be met with. Where complete section of the nerve has taken place the proximal end will usually be found to be enlarged into a bulbous extremity which may be drawn to one or other side of the true anatomical line of the nerve and may, in fact, be intimately adherent to muscle, periosteum or the neighbouring artery. The upper end of the distal segment may show slight enlargement or may merely taper off into the fibrous mass enclosing it. In such a case, there can be no question that resection and suture of the nerve must be undertaken.

In undertaking the *resection of the nerve* it is useless to attempt to join any segment which is still blocked by fibrous tissue and it is, therefore, necessary to make successive sections of the proximal end with a sharp knife blade until small healthy nerve bundles can be seen to stand out clearly without any intervening areas of fibrous tissue. A surgeon may feel disinclined to resect the proximal end extensively owing to the fear that he may not obtain approximation of the nerve ends, but there can be no valid reason for carrying suture through fibrous tissue which will still block the regenerating axis cylinders from finding their way through. The small nerve bundles should stand out as individual fibres and the sheath enclosing them should only be loosely connected to the nerve. Any nerve which shows adhesion to the perineural sheath is still in a condition of fibrosis. In the distal end no nerve bundles will be seen and it is only necessary to remove the fibrous end without successive sections. Every effort should be made to *prevent axial rotation of the nerve* in the hope that in a mixed nerve the motor elements may find their way into motor channels and sensory to sensory. This sounds simple but every surgeon will realize the difficulty in carrying it into effect when he considers the amount of destruction of the nerve ends which may occur in the cicatricial mass in which it is enclosed; and I feel that some of the poor results obtained after operation are due to the fact that motor axons have found their way into sensory channels and vice versa. Difficulty in obtaining approximation of the two ends may be overcome by flexion of the joints above and below, but the wide exposure of the nerve above and below the lesion will in the majority of cases allow approximation to take place.

For suture material I prefer the very finest linen thread or the finest silk, size No. 160, and, although I frequently make use of a stay suture to approximate the two ends together, I rely more upon a succession of interrupted sutures placed around the nerve

through its sheath, taking care that the sutures are not tied tight enough to produce any bunching of the two ends together and often leaving a small space between the two ends. Every attempt should be made to join the nerve by its perineural sheath, as it has been shown that any suture being passed through the body of the nerve may produce some fibroblastic reaction with the formation of a minute central neuroma. In some cases where there has been tension in apposing the two ends, I have been constrained to leave the stay suture in position, but wherever possible would remove it. Before the nerve has been sutured I consider it necessary to remove as much as possible of the fibrous scar left in the vicinity of the repair in order to leave the rejoined nerve in a new bed of fresh muscle tissue. In my earlier work I was in the habit of enclosing the new nerve in a sheath of Cargile membrane or fashioning a graft of fascia or muscle from surrounding tissues, but I now consider this to be unnecessary. In operating upon cases in the musculospiral nerve or in the ulnar nerve behind the internal condyle of the humerus, I would, however, advise the formation of a muscle flap to be placed between the nerve and any bony prominence. *Complete hæmostasis in the area of operation* is most essential, as any effusion of blood after the operation merely leads to the formation of new fibrous tissue. I do not like the use of a tourniquet especially in the arm, and in recent cases I have made use of diathermy coagulation of small bleeding points as a better method of hæmostasis than ligature.

There remain a number of cases in which, on tracing the nerve into the cicatricial mass, a localized thickening will be found on one side with dense fixation to neighbouring tissues, whilst part of the nerve may appear to be intact. In some of these cases direct faradic stimulation may elicit a response in some of the muscles supplied by the nerve, even though clinically none can be obtained, and the surgeon may be in doubt as to whether complete resection is necessary or whether the separation of this localized thickened mass will suffice. I look upon this type of injury as due to partial section of the nerve, and if histological examination be made of the lateral mass it will be found to consist of a conglomeration of axis cylinders which have been prevented from finding their sheaths in the distal segment by fibrous tissue. In this type of injury the perineural sheath has been opened and, in my opinion, the apparent continuity of the nerve will be so affected by endoneural fibrosis that it is probably better to carry out a complete resection than to be content with removal of the lateral scar and partial resection. The one exception I would make to this, however, is in the trunk of the sciatic nerve where the internal and external segments can be often separated into two component parts, one of which may require resection whilst the remaining one may be looped and not require to be divided. It is here that the experience of the surgeon must be brought into play and any marked thickening and undue hardness of the nerve should be an indication for resection.

In some cases the trunk of the nerve may appear to be intact with only comparatively small adhesions to the surrounding structures, but there is a fusiform spindle-shaped enlargement of the nerve which I consider to be due to intraneural fibrosis and probably the result of intraneural hæmorrhage. In these cases I was at first in the habit of dividing the sheath of the nerve longitudinally and dissecting it from the swollen nerve bundle, but I never made any attempt to remove fibrous tissue from between individual nerve bundles as was advocated by the German surgeons. If this spindle feels indurated and if the clinical syndrome is one of complete obstruction, I now think it is better to resect the nerve and make end-to-end suture than to be content with a dissection of the sheath.

Occasionally I have found small metal fragments embedded in the nerve—chiefly in the ulnar in the region of the elbow. These have caused pain in the distribution of the nerve on touching the injured area or on movements of the elbow. In one case a metal fragment was found embedded in the inner cord of the brachial plexus causing a complete block of conduction from which recovery was complete eight months after removing the fragment. I have removed fragments of bone from the sciatic nerve at its exit from the pelvis, from the anterior crural nerve and from the musculospiral, whilst in one case I found a localized swelling in the sciatic nerve to be an old hæmatoma.

It is a recognized principle that all scar tissue in the area should be removed as well as any perineural adhesions which may be found in order to restore the injured nerve to a bed as normal as possible, and it follows that *neurolysis will form the commencement* of every exploration of a nerve. Will this mere freeing of a nerve ever be enough to restore the conductivity and function of a nerve? In other words, will the removal of a scar

compressing a nerve restore its function? Were this so, we ought to see the comparatively rapid restoration as is seen in civil cases of nerve compression. It is more usual, however, after neurolysis to see very slow recovery, and this is probably explained by the intraneural fibrosis which accompanies a gunshot injury following sepsis in the wound. The new vascularization of the nerve in the freshened bed might help, but this is doubtful. Souttar has suggested that the effect of neurolysis is to restore the mobility of the nerve trunk in the tissues and thus prevent the repetition of frequent trauma to the nerve on movement. The decision whether to be content with neurolysis must depend upon the judgment of the surgeon; where the nerve area feels hard and unyielding I would advise resection and only be content with neurolysis where a large portion of the nerve appears to be intact and there appears to be a strong prospect of recovery. There is one point with regard to nerve suture that I would ask for the experience of surgeons who have been fortunate enough to use it, and that is the use of fibrinogen plasma. Personally I have had no experience of this.

There remain cases where considerable *difficulty may be met with in obtaining approximation of the two ends,* although with wide exposure of the nerve and with flexion of the joints a space of three or more inches can usually be overcome without undue tension, the limb being gradually straightened after a period of three or four weeks when union should have occurred at the suture line. Some surgeons advocate in difficult cases that the two ends of the nerve should be joined together by tension sutures, after which the limb is gradually straightened and further subsequent operation made upon the nerve, but I have had no personal experience of this two-stage operation. In two instances a large gap may be overcome by altering the anatomical position of the nerve, and it is frequently useful to transplant the ulnar nerve to the front of the internal condyle of the humerus and the musculospiral nerve to the front of the humerus in order to obtain better approximation.

I would never advocate *shortening of a limb by resection* of a bone in order to obtain approximation of the nerve ends. The only condition in which I consider this justified would be in a case of a musculospiral nerve with an ununited or malunited fracture of the humerus, and even in this event I consider it better surgery to carry out the operation on the bone and leave the operation on the nerve until a subsequent occasion. If the fracture of the humerus has been due to a gunshot wound there is a risk of recurrent sepsis when an operation is to be carried out on the bone, and we know that infective organisms may remain dormant in gunshot wounds and cause a considerable flare-up when any operative procedure is carried out. I would condemn at once any attempt to shorten the bones of the forearm or in the leg.

There are occasional cases in which the utmost ingenuity of the surgeon fails to bring the two ends together owing to the extensive loss of the nerve which has occurred in the original injury. Various measures have been advocated to deal with these cases, and I would at once condemn any attempt to obtain union by means of a *flap carried down from the proximal segment.* I cannot conceive how any surgeon should think that regeneration of axis cylinders can take place after such a manœuvre. Similarly I would condemn any *lateral method of nerve grafting* of one nerve into a neighbouring nerve, by which means the distal end of the nerve is inserted into an incision carried partially through the trunk of its neighbour, as the partial section of the recipient nerve must cause damage to its peripheral supply. I am aware, however, of such cases which were described by the late Mr. Joyce in which apparent recovery had occurred after grafting both the proximal and the distal ends of the ulnar into a partially divided median nerve, a procedure which Mr. Joyce described as "autogenous pedicle transplant". In one case in which I carried out this junction to overcome an interval of 3½ in. there was faradic response in the ulnar muscles after fourteen months. I would, however, not condemn with the same certainty operations by which the ends of the nerve are joined by *autogenous grafts* sutured in such a manner as to fill the gap with approximately the same calibre as the recipient nerve using a piece or pieces of such a nerve as the radial or internal cutaneous in cable form. Records of success have been published by French surgeons, by Joyce and by Forrester-Brown, and I have carried out this cable graft on eleven occasions, three of which showed definite signs of recovery, but the remaining eight were all failures in cases observed from eighteen months to three and a half years. Platt condemned nerve grafting until he saw a case which, on re-exploration gave a definite response to direct faradic stimulation on the proximal side of the graft, and it would be very interesting if, during the

present war, further results could be seen of this method. The best result I personally obtained from a graft operation was one in which two grafts of 1½ in. in length from the radial cutaneous nerve were inserted between the divided ends of the posterior interosseous nerve.

In one case of complete section of the ulnar nerve in the forearm in which a gap of 1¾ in. remained and in which I was unable to approximate the two ends of the nerve by direct suture, I made use of a segment of vein, inserting the two ends of the nerve in a completely detached length of vein and suturing each end of the latter to the nerve sheath. This patient showed a voluntary action and faradic response in the first and second dorsal interosseous muscles after seven months and some return of sensation in the ulnar area of the palm of the hand.

In cases of nerve injury, besides the coincident damage to muscle and bone, it is not infrequent to find that the *main artery of the limb has been ligatured* at the primary operation on the wound. This arterial ligature may produce a certain amount of fibrosis in the muscles from ischæmia and I would like to know if any difference had been noted in the results obtained after nerve reunion in cases in which the main artery of the limb had been previously tied, as I have a feeling that the results were not so good in these cases. During the last war I saw several cases in which compression of the nerve had been caused by an aneurysm in the immediate proximity and this seems to be particularly liable to occur in injuries to the brachial plexus at the level of the clavicle.

There remain a few cases in which approximation of the ends is quite impossible or in which there has been so much tissue damage that nerve repair holds out little prospect of success. These are most frequently seen in musculospiral or peroneal injuries, but fortunately in musculospiral injuries such excellent results can be obtained by *transplantation of* the flexor to the extensor tendons that this procedure may be adopted. With a peroneal nerve so little ultimate disability occurs that it can be easily rectified by an orthopædic apparatus, but in these cases some such operation as tenodesis may be undertaken.

With regard to the *results obtained after operation*, it is very difficult to speak, as so many of our cases were transferred to other hospitals or even to Canada or Australia and we necessarily lost sight of them. However, during the last war we transferred a number of these nerve cases to special convalescent homes where they were supervised and adequate physiotherapeutic measures could be continued. As a rough estimate, about 70% of cases showed some signs of recovery. There can be no doubt that injuries of the musculospiral nerve recovered better than any other and this is probably due to the fact that this particular nerve is mainly motor in function, supplying large muscles. In most cases voluntary action would return in the supinator longus, the extensors of the wrist and in the common extensors of the fingers, but it was not always a complete voluntary action which could be obtained in the extensor longus pollicis muscle. The next most favourable nerve is the peroneal, although the tibialis anticus muscle may be a long time in showing voluntary return. The results obtained after suture of the ulnar, median and sciatic are disappointing. I have seen perfect recovery following in each of these nerves but I look upon it as exceptional. The ulnar may recover as far as proximal muscle supply is concerned and there may be voluntary recovery in the interossei, but it is seldom that the hand will regain its finer movements and co-ordination of movement is poor. This does not matter very much to a man who works as a manual labourer but is a very severe injury to a man who works with his fingers as a pianist, typist or violinist. The median nerve may recover in its proximal muscles but it is seldom that the patient will regain sensation in his index finger, which is a severe disability. Injury to the trunk of the sciatic or posterior tibial must be looked upon as severe, as the patient is so often left with an anæsthesia of the sole of the foot with wasting of the intrinsic muscles and a flexion deformity of the great toe.

Causalgia—i.e. those cases of severe pain in the sensory distribution of the nerve often associated with little paresis of the muscles. These cases are fortunately uncommon, but they are very characteristic. During the last war I saw 33, but so far have seen none during the present war. These were distributed as follows: in the median nerve 15 cases, sciatic nerve 9, ulnar and posterior tibial 4 of each, and one in the radial.

The pain is really severe, brought on in spasms by emotion, or surprise such as a sudden noise, and the patient is most apprehensive of any palpation of the affected area. He will hold his hand swathed in cold, wet towels as heat seems to increase the pain. The

sensory area is pink or purplish in colour and sweating is profuse. The pain may convert the patient into a nervous wreck, increased perhaps by the amount of morphia given him for its relief. I advised operation as soon as the risk of sepsis was over and often at operation there was only slight perineural adhesions to the neighbouring tissue. Neurolysis and removal of the perineural sheath often relieved pain, but in some cases it returned with lessened severity in a few weeks. In two cases of severe pain, injections of alcohol 90% failed to relieve the pain and in one of these it was not relieved by a section and resuture. I operated upon 29 of these cases and the relief obtained by neurolysis was good in 15, and it seems to me justifiable to carry out a simple operation in the first instance but to be prepared to carry out a resection of the nerve at a later date should the relief of pain not be maintained. It certainly seems to be a severe measure to resect the nerve when neurolysis may cure the trouble in roughly 50% of cases.

Dr. C. Worster-Drought: During the later years of the last war (1914-19), while acting as Neurologist to the Woolwich Military District, I examined personally the 1,602 patients with nerve injuries, comprising 1,944 actual nerve lesions to which Mr. Swan has referred (Worster-Drought, 1921*a*). I now propose to consider only certain aspects of this somewhat large subject.

In dealing with cases of nerve injury the routine procedure was to submit all cases for periodical neurological reports. Systematic examination was carried out—sensory, motor, autonomic, trophic and electrical changes being noted for future reference and comparison. A test of the electrical reactions is essential in all cases, not only to assist in determining the severity of the nerve lesion and the necessity or otherwise for surgical operation, but also to distinguish organic paralysis from hysterical. Not infrequently, a hysterical palsy complicates a wound of a limb quite apart from nerve injury and even when one of the main nerves has sustained damage—resulting in anæsthesia and muscular paresis of the area it supplies—a more extensive paralysis and anæsthesia of hysterical type may be superimposed upon the organic disability. Although such a condition may be suspected from the type of anæsthesia and paralysis, electrical examination is the only means of proving the diagnosis, that is, by the fact that some of the paralysed muscles (those hysterically affected) show normal electrical reactions.

For electrical testing I found the Lewis-Jones condenser set most useful. At first I used this apparatus merely as secondary to faradism and galvanism but very soon, becoming impressed with its value, I relied almost exclusively upon condenser reactions. The faradic coil is not an accurate instrument for testing muscle reactions as the factors upon which the contractile response depends—voltage, duration of each electrical impulse, rate at which the impulse is delivered—are very variable and, further, many cases of nerve injury fail to show any response to the faradic coils in clinical use. Galvanism, as ordinarily used for testing, is similarly inaccurate. In the condenser set the voltage is fixed at 100 volts and the duration of each impulse is known; provided that the same precautions are invariably taken to minimize skin resistance and pads of the same size are always used, we have a fairly accurate means of testing muscle reactions and one which is valuable for comparing observations made at different times in the same case in the estimation of progress. I worked out standards of normal reactions which were found to vary in different muscles according to the size of the muscle and the depth of the motor points from the skin surface. These details together with observations on the results of condenser-set reactions in nerve injuries were published in the *British Medical Journal* (Worster-Drought, 1920). In general, no definite conclusions can be drawn from condenser tests made within one month of the infliction of the nerve injury. In certain cases of injury to mixed nerves, although motor paralysis and sensory loss over the area of cutaneous supply may be found more than a month after the injury, the nerve may still recover its function apart from operation. It is in these cases that condenser tests are of great value. In the case of certain injured peripheral nerves (e.g. musculospiral, median, sciatic and its popliteal branches, and anterior crural nerve), if it is found that the majority of the muscles react on or below No. 7 stop, an incomplete lesion may be diagnosed and recovery almost certainly expected without operation. In cases in which the affected muscles (normally reacting in No. 1 or 2 stops) do not respond below No. 8 stop, physiotherapy should be carried out and the case re-examined after an interval of six weeks. If no improvement or actual retrogression is then found in the condenser reactions, operation should be advised even though sensory loss affects only a portion of the area supplied by the nerve. At operation the nerve is usually found to

be compressed by scar tissue or partially divided. If the paresed muscles fail to react on any stop below No. 10—the majority reacting on No. 10 to No. 12 stops—the nerve is unlikely to recover apart from operation. If no response is obtained even on No. 12—the highest stop—the nerve has usually undergone physiological or even anatomical division and will not recover apart from operation. It is not, of course, possible or necessary to distinguish between anatomical and physiological division, but I have found that relatively few cases in whom subsequent operation has shown a complete anatomical division of the nerve, will yield a response on any stop below No. 12 (the highest) at 100 volts in any muscles supplied by the injured nerve. In the lower limbs, the muscles usually fail to show a response even on No. 12 stop when the nerve is completely divided.

By adopting a routine method of examination, including careful estimation of motor, sensory and trophic abnormalities—aided by condenser tests—one was usually able to arrive at a definite opinion as to whether operation should, or should not, be undertaken. Although some cases might have done even better with operation, Mr. Jocelyn Swan exposed very few, if any, nerves in which operation was not indicated. This result I attribute mainly to practice and experience with the condenser set.

As regeneration of a motor or mixed nerve proceeds, there is usually a progressive diminution in the capacity of the condensers, i.e. a gradual lowering of the number of the stops required to evoke a contraction in the muscles supplied by the damaged nerve. For some time—usually four to six weeks—following an operation on a nerve, there is frequently an actual retrogression in the condenser reactions as compared with those taken immediately before operation. Following this interval, however, when the condenser reactions improve progressively month by month, it may be safely assumed that recovery is taking place in spite of the continued absence of voluntary movement. It is not suggested that one should rely solely on quantitative condenser reactions, however great their value, in the estimation of progress; there are other important factors that also have to be considered such as the condition of the paralysed muscles, the absence or otherwise of systematic treatment, sensory changes, &c.

My experiences led me to favour early operation, that is, within six months of complete healing of the wound. There is nothing to be lost, however, by exploring a damaged nerve which has failed to recover, however long the interval from the time of the wound. Cases are known to have recovered as a result of nerve suture performed up to seven years after injury. Cases in which primary suture of divided nerves had been performed shortly after the infliction of the wound invariably had to undergo operation and often resection with secondary suture owing to the intermediate development of sepsis. Nevertheless the primary suture was valuable in having kept the ends of the divided nerve in close proximity.

Following operation, systematic treatment by means of suitable splinting, passive movements of the joints, radiant heat and massage for the affected muscles is essential, and electrical treatment—especially galvanism when the nerve has been completely divided—is of definite value.

As regards nerves that had undergone complete anatomical division, the result of suture appeared better in those nerves containing more motor than sensory fibres, e.g. the musculospiral and external popliteal nerves. This result may partly depend upon the diameter of the nerve, i.e. that the prognosis following suture is better in nerves of smaller diameter. I doubt if the median, ulnar, sciatic and internal popliteal nerves ever recover completely, especially as regards their sensory functions, as a result of suture following complete division. I cannot recollect having seen a single case that showed good recovery as a result of bridging a gap between the two ends of a divided nerve by grafting a piece of nerve from elsewhere in the body. I am aware that fairly good results have been reported from autogenous grafts in the case of certain nerves and especially the facial nerve; possibly results may be better with the more recent method of using fibrinogen in plasma. If centres for dealing with nerve injuries are being formed I would urge the adoption of some systematic scheme for following up the cases—especially those submitted to operation. Satisfactory evidence of good or partial recovery can only be assessed on examination by an expert. The only definite criteria of recovery are return of sensibility to test-stimuli within (not only at the border of) the previously anæsthetic area, and the assessment of voluntary movement and the electrical reaction of each individual muscle.

The posterior tibial nerve.—During the last war I found that injuries to this nerve were frequently overlooked, no doubt because they caused no striking paralysis, all movements at the ankle-joint being normal. More especially do they escape recognition when the lesion lies below the point of origin of the branches supplying flexor longus hallucis and flexor longus digitorum as in such instances power of flexing the toes is retained. In all wounds involving the calf associated with a complaint of pain or weakness in the foot, a systematic examination should be made of sensation in the plantar area and of the functions of the intrinsic muscles of the foot. I met with no less than 64 cases of posterior tibial nerve injury, most of which were referred to me as suffering from a "functional" disorder. Observations on these 64 cases were published in 1921 (Worster-Drought, 1921*b*).

When the posterior tibial nerve is damaged, changes in cutaneous sensibility—varying from over-reaction to complete cutaneous anæsthesia according to the degree of injury—will be found over the sole, at the margins of the foot, and over the posterior and lateral aspects of the heel. Sometimes there are sensory changes, varying in different cases, over the dorsum of one or more of the toes. There is also paresis and often atrophy of the plantar muscles and interossei, the toes being hyperextended at the metatarsophalangeal joints and flexed at the interphalangeal joints. Flexion of the toes, and occasionally extension, may be less complete than in the opposite and normal limb.

When the site of injury is above or involves the branches of the posterior tibial nerve supplying the flexor longus hallucis and flexor longus digitorum muscles, flexion of the toes is either much diminished or is entirely absent. The ankle-jerk may also be reduced or impossible to elicit. On faradic stimulation of the posterior tibial nerve on the inner side of the tendo Achillis, the response in the plantar muscles will be greatly diminished or absent. Similarly stimulation of the motor points of the affected muscles shows a reduced or absent reaction to faradism, and a response only to the higher condenser stops—No. 8 (0·5 microfarads) to No. 12 (4·0 microfarads) at 100 volts Lewis-Jones scale—or in complete lesions, no reaction even with the highest capacity (No. 12—4·0 microfarads).

Tinel's sign.—The gentle tapping with a light percussor or one finger along the course of the nerve distal to an injury is said to give rise to paræsthesia if regenerating nerve fibres are present. If the point at which percussion produces paræsthesia gradually extends down the nerve, month by month, regeneration can be assumed to be taking place. I found Tinel's sign of little value. It is certainly present in some regenerating nerves but in others it may be found without apparent recovery while, in nerves deeply situated, good recovery may ensue when the sign has been absent throughout the period of regeneration.

Causalgia.—This painful lesion occasionally complicates injuries of the median and internal popliteal nerves especially. The ulnar and external popliteal nerves are much more rarely affected. The pain is of an intense burning character often relieved temporarily only by the application of cold water or the keeping of the affected limb wrapped up in a wet towel. Many forms of treatment have been employed in the attempt to relieve causalgia: Galvanic baths; deep X-ray therapy; injection of the nerve with alcohol above the lesion; section of the nerve above the lesion with or without resection of the damaged portion; section of the corresponding posterior spinal nerve roots; peri-arterial sympathectomy above the lesion (e.g. axillary artery for median nerve causalgia); cervico-thoracic sympathectomy (extirpation of the portion of the sympathetic trunk including the inferior cervical ganglion and the first and second thoracic segments); and lumbar ramisectomy.

I have seen all the above methods of treatment applied and have seen all of them fail to relieve the symptoms. Resection of the damaged portion of the nerve appeared to give the best results, by diminishing but not necessarily abolishing the pain. Sympathectomy also brought about some degree of relief in a few cases.

According to some authors, causalgia continues for a varying period up to two or three years and then tends to disappear. This is not in accordance with my own experience. In spite of nerve section and partial resection, some of these unfortunate patients continue with their symptoms and gradually sink into a condition of profound psychoneurosis and become drug addicts; others develop an ascending neuritis. One such case I saw continued for nearly seventeen years—in spite of early section of the posterior spinal nerve roots and peri-arterial sympathectomy—and then died from an intercurrent malady.

REFERENCES

WORSTER-DROUGHT, C. (1920), *Brit. M. J.* (ii), 389.
Id. (1921*a*), *J. Roy. Army M. Corps,* **37**, 386.
Id. (1921*b*), *Brain,* **44**, 54.

Mr. Rowley Bristow, discussing the question of technique, reminded the meeting that the positioning of the limb was all important in obtaining end-to-end apposition after removal of end-bulbs, preceding the suture of a nerve. He stressed that in suturing the sciatic, in addition to flexing the knee, extension of the hip was a manœuvre of some value. In suturing a median, by flexion of the wrist one gained about 1½ in., whilst positioning the limb, together with transposition to the front of the elbow enabled a gap of some 6 in. to be overcome in the suture of the ulnar nerve.

Mr. Bristow deprecated the use of a stay suture, that is one transfixing the nerve, and also opposed any question of wrapping with membrane, fascia or fat.

He described the neat bi-polar electrode given to him by Dr. G. L. Brown which is used in testing an exposed nerve with the faradic current—a test which the surgeon should always be prepared to carry out at operation and which, in difficult cases, might well prove to be the deciding factor as to whether or no resection and suture should be performed.

Mr. Bristow said that the results of grafting as seen in the last war were poor. Whilst further improvement in technique and the use of fibrinogen plasma might add to the efficiency of the method, yet the two-stage operation, that is suture of end-bulbs under tension, the posturing of the limb, the gradual stretching and then some two weeks later a second operation and end-to-end suture, was still the method of choice. He deprecated the use of a graft at the present time unless every effort to produce end-to-end suture, including the two-stage method had been tried and failed.

He would suture a divided nerve in a clean wound, or following a primary debridement, if the patient came under his care within the first few hours and the chances of first intention healing were good.

He stated that in his experience complete neurological recovery following suture was rare, but useful recovery of function was likely following successful suture. Finer movements, particularly of the small muscles of a hand were unlikely to be regained, but recovery of gross sensation and recovery of movement in the proximal muscles was to be hoped for. Following the last war, great difficulty had been encountered both in this country and in America in following up the true end-results of the patients with nerve injuries. Under the ægis of the Medical Research Council and by the segregation of the Service patients into three centres, it was hoped that a follow-up survey would, on this occasion, yield more fruitful results.

It was the intention of the Medical Research Council to follow up a considerable number of patients for a period of five years with accurate records and with observations at appropriate intervals in order that we might ascertain the true state of affairs as regards prognosis and recovery with individual nerves.

In the treatment of causalgia, peri-arterial sympathectomy as advocated by Lériche had not been successful in the hands of the British surgeons. In the milder cases, neurolysis and the freeing of the nerve from surrounding scar tissue or from the pull of a tendon to which it had become attached, sometimes gave a satisfactory result. In those in whom the symptoms were severe and who failed to respond to symptomatic treatment, or neurolysis, resection and suture was called for. This relieved the symptoms but he had known patients in whom the symptoms recurred as the nerve proceeded to regenerate. He believed that these patients improved with time just as do patients with painful phantom limbs following an amputation. Causalgia is rare. With some 200 patients in the centre in which he worked, there was only one patient with causalgia and he had only seen three during the present war though milder degrees of pain, with incomplete or irritative nerve lesions, were common.

[*See also* page 513, Section of Orthopædics.]

Section of Psychiatry

President—C. P. Symonds, M.D.

[*March* 25, 1941]

Psychiatric Aspects of Effort Syndrome

By Aubrey Lewis, F.R.C.P.

The term *effort syndrome* according to the report of the Medical Research Committee (1918) covers all persons in whom breathlessness, pain, exhaustion, giddiness and fainting are experienced for the most part during, or after, exertion. In practice, however, the term *effort syndrome* is applied only to those "in whom no physical signs of structural tissue change are discovered". From the standpoint of physical medicine enough has been done when this eliminating procedure has been carried out; the term *effort syndrome* seems an adequate diagnosis for those cases of *effort syndrome* in which it is not symptomatic of physical disease. It is hardly to be expected, however, that the psychiatrist will be content to stop there. It is as necessary to classify in terms of psychiatric categories where these can be detected, as in terms of physical disease. In the report of the Medical Research Committee it was said: "The term *effort syndrome* is non-committal on the pathological side; it expresses a fact of which there is general recognition, namely that the chief symptoms are unmasked or aggravated by exercise; it generalizes many phenomena of the malady in that these are no more than exaggerated manifestations of healthy responses to effort." If for "pathological" one substitutes "psycho-pathological" and for "exertion" or "effort" one substitutes "emotion", this statement applies well to the psychiatric position, so far as the nature and classification of the syndrome goes. It is significant that although *effort syndrome* received a good deal of attention towards the end of the last war, and for a few years afterwards, the term rapidly dropped out of use, and has been revived more, one must suppose, because of the administrative necessity of singling out those men in an army who become distressed on exertion, than because it stands for a unitary condition or a diagnosis which is of value in indicating prognosis and treatment. Since, then, the definition consists of a description of the symptoms, with a qualifying clause about effort, there need be no dispute about the symptoms. The defect in the definition is that it does not include symptoms of an explicitly psychological kind. The psychiatrist, accustomed to his systematic examination of the mental state, finds the official description of symptoms inadequate and may therefore be pardoned if, after having seen many such cases, he concludes that a disorder in which breathlessness, giddiness, palpitation, headache, excessive sweating, tachycardia and tachypnœa, and tremor are conspicuous or often occur in paroxysmal attacks, is an anxiety state. So often the patient who came during peace time for treatment of his anxiety state, stressed at first the physical side of the matter because he thought that was what the doctor would be interested in.

Before considering into what categories the soldiers with *effort syndrome* fall, it is perhaps worth while examining the view that because there is no physical disease this must be a neurosis, or on the other hand, that because there are physical phenomena, or what might be called physiological symptoms, this cannot be a neurosis. Taking one's standpoint on the indivisibility of mental and physical happenings, and on the indivisibility of mental disorder, whether for convenience it be called neurosis or psychosis, it is plain that the discovery of metabolic or other "physiological disturbances of function" does not prevent us from regarding an illness as predominantly a mental disorder, any more than a post-encephalitic, post-traumatic, or post-paretic behaviour disorder ceases to be a mental illness, because of its physical substrate. Cyclic schizophrenia, phenylpyruvic oligophrenia and hysterical vomiting or emotional diarrhœa, are all in the psychiatrist's province.

There is so widespread a belief that anxiety is the common accompaniment of such somatic phenomena as we are here dealing with—breathlessness, palpitation, excessive sweating, diarrhœa and other symptoms of vegetative disorder—that it is possible to overlook other affects. Depression is the commonest of these. Half of the patients report depression; more or less persistent, and of a degree that may be called morbid. "I feel just like jumping over the top of the banisters. I felt absolute despair. I think that everything in the world is hopeless. Lately, I haven't hit it with people, I imagined things

about them, I wondered if they had any use for me, wanted my company." "I get quite depressed. I have less interest. I can make some effort but I don't enjoy it. My appetite did fall off, I can't concentrate. I find it very difficult—even reading." "In barracks I got in the dumps. And I got diarrhœa at the time. I used to wish I was dead when I had this. I did absolutely, no doubt about it. But I'm better now, I observe birds, I feel interested. I'm not stone dead. I can concentrate but not as well as I could once." "I get turns of depressed feelings, fed-up. I feel as if I want a good cry to clear myself. I have a job to concentrate. My appetite is pretty poor, especially when I feel fed-up. I don't eat at all."

"I have miserable feelings. When I get palpitations very bad I feel life is hardly worth living. I couldn't eat hardly any food." "I don't care a hang what happens." These are typical statements by patients with *effort syndrome*.

It is a point worth insisting on, that fear (or anxiety) is not the only affect which may lead to such phenomena as those of *effort syndrome*. A telling instance of this is the study which two careful observers made of neurocirculatory function in mental disorder. They used the Schneider index, which scores pulse-rate and blood-pressure at rest and their response to exercise. They found that athletes of course did very well: normal controls did well; neurotics and insane people did less well, in the order schizophrenics, manic-depressives, neurotics: but patients with conversion hysteria did better than manic-depressives, and those with anxiety states much the same or a little worse.

It is not, however, by a study of the emotional state alone that the patients with *effort syndrome* can be rightly diagnosed.

From observations on the mental state, previous personality and history of our patients we concluded that they fell into the following categories:

	Per cent.
Anxiety state, acute	17
chronic	14
Depressive state	12
Psychopathic personality	18
Hysteria	11
Post-infective neurasthenic	11
High-grade mental defect	4
Schizophrenia	1

The remaining 12% had organic disease.

This needs some elaboration. The proportion of cases diagnosed as anxiety state was 31, yet over 70% of the patients showed evidence of anxiety. There were only 12% diagnosed as depressive state, yet 50% of the men were depressed. The contradiction here is only apparent. Anxiety and depression as symptoms were very common among our patients, but there is a wide gap between a symptom and a diagnosis. This is not the place to go into the difficulties of psychiatric diagnosis; the patients diagnosed as anxiety state and as depression are those in whom this was an adequate description of their whole condition. 11% of our patients were diagnosed as suffering from hysteria. These were men who exhibited either conversion symptoms, for the occurrence and localization of which the motives could be perceived, or they showed dysmnesic and other hysterical symptoms, often with a history of a hysterical personality before. It would have been easy to classify many of these patients under the heading psychopathic personality, if it were not for the overtly hysterical nature of their symptoms. Those who have been classified as psychopathic personality raise some interesting questions; the majority of them were men who had from childhood shown timidity and aversion from any enterprise which called for sustained effort, whether mental or physical. In some the avoidance of effort had been more selective; they had either avoided games and manual labour entirely, or on the other hand they had been lazy-minded, without initiative, persistence, or capacity to endure the hardness of the mind. Mostly hypochondriacal, their lives could easily be seen as a sequence in which each avoidance of effort had in its turn led to reinforcement of their incapacity. Sometimes these quarter-invalids had seemingly been launched on their career by the injunction of a doctor who had said that the child had a weak heart, and must therefore be guarded against exercise, so that he might grow out of it. Similarly parents with symptoms suggestive or indicative of heart disease had often influenced the child in this direction by solicitude and the fostering of anxiety about bodily health.

The term psychopathic personality is often taken to indicate anti-social trends, if not actual worthlessness; this was not so in the men whom I have designated by the term.

It is not denied that among soldiers with *effort syndrome* an attitude not far removed from that of a delinquent is to be found, and is intimately connected with the promotion of their symptoms, or with the exaggeration of these. But it is possible to feel incapable of physical exertion, whilst still capable of excellent work in various directions. Our men with *effort syndrome* were no more asthenic, judged by an index which is a reliable indication of asthenic physique, than the men of the infantry regiment, whom we also examined at the neighbouring barracks. The much larger series of measurements which my colleague, Dr. W. L. Rees, is making may invalidate the conclusion drawn from this statement, but even if the skeletal structure of these men differs from that of an average group of healthy men of their age, I should still hesitate to think of their constitutional predisposition, such as it is, in mainly physical terms, unless a prominent disorder of some physical function, relevant to their symptoms, could be demonstrated: anomalies of vital capacity, say, might be such a characteristic, but I know of none so far demonstrated. Equal caution is necessary in dealing with psychological attributes for which we are largely dependent on hearsay reports or on the man's own highly biased account. Intelligence level is much the same in these men as in any other group of soldiers.

Constitutional effort syndrome is a convenient term perhaps for referring to those men who have shown the symptoms for a great part of their lives, and who have physical and psychological characteristics in keeping with the conception. In saying they have had symptoms all their lives, it is not to be supposed that incapacity for ordinary work is implied, much less actual illness. These men have so ordered their lives that they have disregarded or circumvented what symptoms of *effort syndrome* they experienced and, for the most part, they have never dreamt of going to the doctor about it. They have belonged to that large group of more or less neurotic people who get along very well with their symptoms, under the ordinary social conditions of living in this country, and whom it would be a mistake to treat or to encourage to seek treatment. This mistake unfortunately has been made, only too often, when the men came into the Army. It is true that in some of them the unusual requirements of Army life have led to so much distress that their symptoms were obvious and quite incapacitating. But there are many others who would have been able to carry on perfectly well, so far as one can tell, if their symptoms had been ignored, and, still more important, if they had not been sent to hospital and overhauled repeatedly, sometimes with the erroneous diagnosis of heart disease in one form or another tacked on to them.

It would not be unreasonable to ask why I have singled out a particular group of these men as suffering from psychopathic personality, when so many others among the patients doubtless had anomalies of personality which could be described in such categories as obsessional, depressive, hysterical, anxious, sensitive, or, more simply, in the three categories of psychopathic personality which Professor Henderson has so lucidly described in his Salmon lectures. It might even be questioned whether any systematic diagnosis in terms of personality should not be made to include, let us say, the schizophrenic patient and the relatively large group labelled post-infective neurasthenia. This is a logical and theoretical objection, to which there is no reply, except that of experience. If there was among our patients a group in whom there had been no particular indication of proneness to effort symptoms, before the occurrence of an infectious illness, and if their symptoms tended to subside, without any positive psychiatric intervention, and not to recur under conditions of considerable stress, then it would seem expedient to classify such cases as post-infective, rather than in terms of their previous personality, whether it fell within the narrower range of the norm, or exhibited some inconspicuous psychopathic traits. There may be some question about the number of such men, but hardly about the expedience of the procedure. There is a practical difficulty which seems to me to preclude any attempt to differentiate these men at all satisfactorily in terms of personality. There are three sorts of data on which we assess personality: the man's statements about himself; statements by his friends and acquaintances; and our observation of his behaviour—perhaps one should add as a specialized instance of the latter the results of psychological tests (such as the Rorschach, thematic apperception, &c.). None of these is satisfactory. As to the first of them there is abundant evidence to show that it is always partially unreliable, and often grossly misleading. Not only are there the usual difficulties that arise when anyone tries to paint a picture of his own character, but there are in these men motives, both conscious and unconscious, for distorting their account, which make one reluctant to accept at face value what they tell of themselves; this is of course not a flat indictment of the information a man may give about his past habits and

qualities, but it renders such material very dubious for any serious study. Ideally one might be able to separate fact from fantasy, and utilize fantasy too, in evaluating a man's personality, but, practically, this presents enormous difficulties in many cases, and yields, at best, a one-sided picture of the man as he sees himself, and as he reveals himself. Adequate information about him from others is necessarily hard to come by: and our observation of his behaviour is limited by the somewhat artificial nature of the hospital environment. Caution and experience moreover prevent one from assuming that the features the man exhibits during a neurotic illness are to be taken outright as exaggerations of his ordinary personality traits. So far as the Rorschach, and any similar psychological tests are concerned, this is a matter of research still, and the material we have so far obtained does not justify any statement as to the types of personality. Dr. Wittkower has kindly sent me the data he and his colleagues are shortly publishing. Relying on the men's autobiographical statements, they found that of their 50 subjects almost all showed obsessional traits. It is proper that I should indicate that we found hardly any obsessional symptoms among our men, and that the proportion of those with a very keen sense of duty and rigid moral outlook was no higher than among the mixed neurotic population of the rest of the hospital.

Treatment and Outcome

Treatment can do much to bring the syndrome to an end as an incapacitating illness. A quarter of the men admitted to this hospital with *effort syndrome* are doing full military duty (on inquiry) six months after discharge from hospital. It is a smaller number than those who are free from symptoms by the time they leave hospital; but where external stresses played a large part in producing the illness one cannot insure the man against further illness if these stresses are again brought to bear. How the men have got on who were discharged from the Army back to civilian life, it has not as yet been possible to ascertain on any representative sample. One would suppose that the majority of them do as well as they were doing before the war.

Graduated exercises are not to be regarded as the very centre and basis of treatment. Regular occupation in the workshops was made as prominent as games and physical exercise in the régime of treatment (giving the morning to the one, and the afternoon to the other), but even so it was clear that one could not, by exercise, build up a man with *effort syndrome* in the way that Milo of Crotona learnt to carry a bull. What emerged as the best treatment was an individualizing treatment: whether the man went to physical training or not, and what he did there depended, not merely on what he chose to do or thought he could do, but on what, after a full psychiatric assessment, seemed the best thing for him to do. In other words, some men were not put on P.T. at all, other men were urged to carry on in spite of much breathlessness or other symptom of the *effort syndrome,* and yet others told to stop as soon as symptoms developed. Similarly some joined in the games more than in regular exercises. We had the advice of Sir Adolphe Abrahams in regard to this; and his expert knowledge of what athletes do, and of what training can do for men who are not athletes, was a standby. It must not be supposed that this is a contradiction of what Sir Thomas Lewis and others have urged in advocating physical training and games in the treatment of *effort syndrome.* It is simply an attempt to put it in psychiatric perspective. Lewis has rightly insisted that the games and exercise serve an excellent purpose in grading the men according to their stage of improvement; if the man cannot do well in these exercises he is evidently incapable of doing well on full military duty. The converse need not hold. It should, however, be conceded that a man may still be incapable of taking part in energetic exercise, yet may be an admirable soldier in certain departments of the Army.

How far is deliberate psychological treatment called for? It would be easy to take refuge behind the common plea or apology that since there is not time for thorough psychological treatment, something not quite so good has to be put up with. I dislike this because it leaves many people supposing that if only "proper" psychological treatment, by which they mean daily or thrice weekly sessions over a fairly long period, could be carried out, all would be well. This is certainly not the case. Neither is it the case that hardly any of the men would benefit by systematic psychological treatment. But there were, as it turned out, few of the patients in whom it seemed reasonable to try the kind of psychological treatment which calls for much unravelling of the patient's past and bringing it into relation with his present. The present often loomed so large, and was so clearly the main obstacle, which could not be talked away. The number thus treated has been small and the results dubious. What can best be called re-education, centering on dis-

cussion of evident problems and emotions, has been employed in a large number of these men, and whether it be classed as persuasion or as psychological talks, it has in practice been of exactly the same kind as a great deal of the psychological treatment given to the more pliant cases of civil life. As to what part suggestion may play, my colleague Dr. Gillespie will have some remarks to offer presently. Reassurance, I need hardly say to a psychiatric audience, is useless if it is merely negative. A man who is convinced that his heart is diseased will not give up that belief because a psychiatrist, or any other physician, tells him he is wrong. I think the attitude of so many of these men expressed in their *idée fixe* concerning their heart can be shown to be catathymic, and at least the psychiatrist must give them some positive explanation in its place, though when it is habitual, or is a quasi-delusional notion, or the canalized expression of anxiety about a vital part of the body, something more than a substitute explanation is necessary. Much might be said here as to the part that the ordinary doctor plays in the causation, and might play in the prevention, of *effort syndrome*. It is easy to overrate the former and overlook the latter. Thus the regimental medical officer has the best opportunities, if only his military and previous medical experience has shown him how much can be done, to avert such a neurotic disability as this by prompt and firm measures. Many of the patients he will not refer to a specialist, nor send to hospital, but will be able by reassurance and unobtrusive guidance to keep on full duty.

The decision as to whether a man with *effort syndrome* should be retained in the Army —and if so in what category—or should be discharged is a difficult one. Freedom from symptoms after treatment is not a reliable criterion by itself. Probably the most reliable in deciding for return to military duty is the combination of freedom from symptoms with willingness or eagerness to go back. It is open to the physician to make a recommendation as regards the work the man should do, or the branch of the Army he should be transferred to on return to military duty. The problem presented by the man who is a vocational misfit in the Army is indicated by the high proportion of sedentary workers among those with *effort syndrome* in the last war, as quoted by the Medical Research Committee's report and Sir Thomas Lewis. They developed *effort syndrome*, I believe, not because sedentary workers can't make physical effort, but because they are unaccustomed to physical labour and dislike it or are frightened of it.

Discussion.—Dr. W. H. GILLESPIE: When a case of *effort syndrome* came into my ward accidentally I decided as an experiment to treat him on the same lines as a conversion hysteric. At the time I felt very dubious about this procedure ; a fact by no means irrelevant, for this subjective difficulty in approaching cases of *effort syndrome* just like other neurotics is one of the things that hampers us greatly at the present time. We ourselves tend to be affected by the old cardiological approach, and so we feel that *effort syndrome* is as it were half-way to being a cardiac disorder, just as the patients do. To treat an hysterical paresis by suggestion is easy and natural ; but it goes against the grain to carry out the same kind of treatment if one feels that the symptom is the result of some obscure physiological dysfunction connected with the vasomotor and autonomic nervous systems.

My approach could be formulated thus: If suggestive measures in a case of *effort syndrome* should bring about a rapid disappearance of the leading symptom, it would be strong evidence that the symptom in question is one of hysterical conversion. It is obvious, of course, that the result is valid only for the case in question, and one would be entirely unjustified in generalizing it. According to Dr. Lewis's figures 11% of the cases were diagnosed as hysteria.

Another difficulty is presented by the vagueness of many of the symptoms in cases of *effort syndrome*. It is easy enough to see whether or not one has cured a paralysed leg ; but where the symptoms are indefinite, variable, and purely subjective the situation is less satisfactory. By looking for somewhat flamboyant symptoms, however, one had a symptom whose presence or absence could be in no doubt, and at the same time one which was more likely to be hysterical.

My first patient fulfilled these conditions. He was a man of 25 of rather simple and credulous type who had marked dyspnœa on slight exertion and constant tachycardia. Always considered delicate, he " hadn't the energy to play football ". He took up boxing at 15 to make himself strong. A year later, when boxing with a man 3 st. heavier he received two heavy blows over the heart and the solar plexus, which knocked him out on his feet, according to his own account. He dates his *effort syndrome* from this event, which he regards as causative. He could do his job as travelling salesman by taking his own time, but in the Army he found it impossible to keep up with the others and became hopelessly out of breath. He felt he was being bullied by the N.C.O.s because he had to take things slowly.

On examination, his resting pulse-rate varied from 100 to 110, and the exercise tolerance test gave: 130 standing, 160 after exercise, 128 after 1 minute. He showed a little dyspnœa even on standing up, and it was very marked after exercise, but lasted less than a minute.

He proved to be easily hypnotized, but at first negativistic in his response to therapeutic suggestions, with a tendency to try to escape from rapport into erotic and sexual dreams. These difficulties were overcome and there was a striking and rapid improvement in his respiratory response to effort, so that after the fifth hypnotic session there was very little dyspnœa. His fear of return to the Army was obviously the most potent factor operating against complete recovery, so at this point he was promised that discharge from the Army would be recommended. He was also given the post-hypnotic suggestion that he would ask for P.T., and he did so. After this, complete symptomatic recovery was uninterrupted and rapid; he reached the highest grade of P.T. three weeks later and maintained this level without any complaint until his discharge, eight weeks after treatment began. His tachycardia, however, was not affected at all by the treatment, although his pulse-rate when asleep was only 70 to 80.

Since this initial success I have been looking for other suitable cases, but various difficulties have appeared. In most cases considered, the symptoms were too slight, or there were some complicating factors.

One patient selected was of athletic type with obvious motivation for his symptoms, wishing to leave the Army and return to the Merchant Service. He stood up very well to twenty-five minutes strenuous P.T. without either subjective or objective distress. Two days later he took part spontaneously in a football match and collapsed on the field shortly after half-time. When seen ten minutes later, he complained of præcordial pain and was dyspnœic, with respiratory rate of 40 and pulse-rate of 120. Dr. Lewis saw him a few hours later, when he was still complaining of pain in the chest, and found he had a hysterical paresis of the left pectoralis major. Dr. Lewis then elicited a circumscribed area of hyperæsthesia over the sternum; he observed in the patient's hearing that he expected to find a "corresponding" area of hyperæsthesia over the thoracic spine, and this was very convincingly demonstrated. The patient's suggestibility was thus firmly established. However, I failed to hypnotize him satisfactorily at the first attempt, but the second was much more successful. He did not complain of any more symptoms after this, but a few days later he fractured a metatarsal bone at P.T., and this mishap interrupted his treatment.

Here is another case, at present under treatment. This man's main symptom, as in the first case, is dyspnœa on exertion, and though slighter, it was very definite after mounting a chair 20 times. After two hypnotic sessions his dyspnœa on taking this exercise had disappeared so completely that I felt tempted to regard the reaction as a supernormal one!

The third case resembled the first one also in that hyperventilation was followed by dyspnœa instead of apnœa. My findings so far indicate that this peculiarity is related to the feeling that overbreathing is violent exercise, and therefore bound to lead to dyspnœa—a very pretty example of an hysterical as opposed to a physiological mechanism. In both cases treatment abolished this unphysiological response.

Effort syndrome is essentially a war neurosis. It is true that the history frequently goes back for a much longer period; but the condition rarely becomes a complaint for which medical advice is sought until the patient enters the Army, and this is only in part because the patient is then subjected to greater physical strain. At least as important is his exaggerated idea of what being a soldier involves. Essentially, he feels that impossible demands will be made on him by an implacable authority. The patient loses sight of the realities of the situation because he is overwhelmed with anxiety related to an archaic phantasy situation in which he is a helpless little child and the Army machine is an all-powerful, cruel and terrifying father. Our task in treatment would be simpler were there never any real justification for this attitude of the patient.

The type of treatment I have been outlining probably produces its effect by allowing the patient to identify himself with parental power as represented by the physician and to feel himself supported by it, instead of feeling that he has to oppose and fight it in the guise of the Army machine.

Dr. JOHN PARKINSON said that he was not yet convinced that a psychoneurotic origin for *effort syndrome* had operated in so large a proportion as psychiatrists claimed. One difficulty was that comparable analyses of other and dissimilar conditions, e.g. valvular disease, or hypertension, were often reported giving psychological histories or troubles much the same (and as frequent) as those reported in *effort syndrome*. He agreed with Dr. Aubrey Lewis that the term constitutional should not be restricted to the physical frame, but should include the nervous as well as the physical component. He had often been struck by the small soldier in a large uniform, slightly and even badly built, yet who possessed spirit and proved to be wiry—and fully capable of his task. The

physical measurements being made at Mill Hill, as a control in those who at first sight appeared to be of poor physique, should prove of interest and value. While admitting that thoughtless and ill-founded suggestions of a " weak heart " were quite capable of initiating a liability to *effort syndrome*, that tendency was surmounted by the average man, leaving only a small proportion in which the syndrome could be attributed to that unfortunate source.

In the extreme demands made upon a civilian become soldier, there was a limit set by his circulatory efficiency which might not much depend upon psychological perfection. The kind of syndrome encountered would vary with the type of warfare waged, and if physical and nervous strain were combined in prolonged hostilities, he feared that *effort syndrome* might become a large problem in this war as in the last.

Dr. W. CLIFFORD M. SCOTT: By showing that effort is of no great importance and by showing that as a syndrome it is a construction of the physician and useless psychiatrically Dr. Lewis's paper has sounded like the obituary of the *effort syndrome*. He has convincingly shown that the cardiologist is helpful chiefly in reassuring both the patient and the psychiatrist that the major task of treatment lies elsewhere than in attempting to treat the cardiovascular system. This represents a change in attitude similar to that which occurred towards the discarded term " shell-shock " during the early stages of the last war when it was later admitted that the neurological implications were rare and secondly that the problem was not that of a syndrome but that of patients whose symptoms ranged throughout most psychiatric possibilities.

Among the patients with *effort syndrome* who have been sent to our unit all the diagnoses mentioned by Dr. Lewis occurred as well as many which came within the " obsessive-ruminative-tension " group of Meyer and within the manic-depressive group. Among the obsessives were many with a variable hypertension. Such patients might profit by treatment planned by the collaboration of cardiologists and psychiatrists as hinted at by Dr. Parkinson.

One of my cases is an intelligent man of 36 who volunteered in November 1939, and lived the healthy life of a driver. He was active in the Flanders campaign though tired. He was occasionally annoyed at seemingly senseless journeys, later ashamed when he realized he was retreating, and finally at Dunkirk with a pal decided he would fight to the death rather than be captured. While lying to avoid a stick of bombs he heard four fall and the fifth wounded his left arm. He remembered thinking that he had lost his legs and regained full awareness kicking. He felt pain in his left chest. He was in hospital till August and his wounds healed well. He remained frightened and the pain in his left chest became worse on activity. He was home for two months where he did not improve. In October 1940 he was admitted to a psychiatric unit where he was found to be physically fit. His B.P. varied between 170-120 S. and 130-90 D. He was easily frightened by alerts and complained that exertion incapacitated him by pain and breathlessness. His one wish was to be discharged and to try to adapt to a life of cardiac invalidism. He tried to lie about his condition hoping he would be discharged. When he did not succeed in this he became openly depressed and felt he would break down mentally. Later he became variable. After four months, one day the pain suddenly lifted " like a cloud ", and he felt elated. He began to be self-reproachful about having volunteered and having left his wife alone. He felt that the lifting of the pain was related to a change in his attitude to his wife and when he later talked of momentary depression his hand moved unconsciously to his heart. He had lived an active life but had always been slightly uncomfortable lying on his left side. He had had a premonition that he would be injured on the right side. Until 22 he had been a professional sprinter. He was in hospital about five months and treated about twelve hours psychotherapeutically.

The second patient is a driver of 22 who was called up, was sent to France and evacuated through St. Nazaire where his pity for the victims of the Lancastria, his fear, his anger " became too much " for him. He continued at duty until palpitation and worry about heart disease led to hospital admission in October 1940. He was tense, communicative and fearful of activity. His B.P. varied from normal to 155/110. Gradually he admitted that his trouble was dated to at least January 1938 when his mother had died and he had tried to hide his sorrow from his sisters of 28 and 34 who had mourned more openly. He gradually improved and returned to his unit with the attitude " I must fight on " but was not able to allow himself many of the pleasures of being a patriot. He was in hospital about six weeks and was treated for about an hour and a half psychotherapeutically. If such patients as these are dealt with as only showing physiological signs of fear much is missed and many therapeutic possibilities are left unexplored.

Dr. WILLIAM SARGANT: Dr. Lewis has asked me to talk about possible hyperventilation symptoms in *effort syndrome*. I have not recently been able to carry out much detailed work on hyperventilation effects in the neuroses. Many of the cases of *effort syndrome* seen by me have been simple anxiety or depressive states in which the

respiratory system has seemed little affected. Hyperventilation effects have been relatively uncommon in this group. In a few other cases, however, some interesting hyperventilation symptoms, complicating the primary picture of tachycardia on effort or excitement, have been seen. Two cases, for instance, had attacks of spontaneous hyperventilation tetany. One of these, sent in with a diagnosis of *effort syndrome*, who could do heavy work down a coal mine, presumably in a raised CO_2 atmosphere, developed symptoms of dizziness in the head and even tetany on effort or excitement when he came up from the pit. His condition was made much worse by Army Service, and I advised his immediate return to pit work, where he seemed to have found his own peculiar adjustment. Lesser symptoms which may be brought on by respiratory alkalosis, such as dizziness in the head, fainting feelings, and general weakness, can easily be missed because they are less dramatic than full-blown tetany, but they are probably commoner. Attempted control of the breathing sometimes helps such a patient when he feels the attack coming on. As a whole, severe cases with these complications have been the exception rather than the rule in the general run of *effort syndromes* seen in the past eighteen months, but in the actual therapeutic attack on an individual case it is only by treating all these aspects when they occur that the best results are achieved.

Dr. MILLAIS CULPIN described how he had been familiar, in the last war, with the faintings and palpitations, the sweatings, tremblings, dyspnœa and general weakness, of men labelled " shell-shock " or " neurasthenia ". Knowing that such symptoms did not arise from disease of the heart he never examined the heart in such cases, having already given up the pernicious gag about " the need for thorough examination of the neurotic patient ". He told the men that the symptoms would get well as their nervous troubles were cleared up, and was startled when he discovered that the patients were clinically identical with those who were labelled D.A.H. and sent to heart hospitals for elaborate investigation. He found that the extensive cardiological writings of the period made no mention of psychological possibilities; in the general war neuroses his search for help from neurology had already drawn a blank. He was then moved twenty years ago, to publish an article with a title almost identical with that of to-day's paper—" The Psychological Aspect of the Effort Syndrome "—which was an enunciation and defence of the theme that there *was* a psychological aspect. It was of necessity amateurish; how amateurish he had not realized till he heard the masterly account of Dr. Aubrey Lewis, but it is none the less a useful indication of the state of opinion in those days. He differed from Dr. Lewis only in feeling that we should have more courage in emphasizing the harm that is done, both in the Army and civil life, by the faulty handling of such cases.

Major H. V. DICKS regretted the absence of Dr. Wittkower who, with Majors Wilson and Rodger, was about to publish a paper on the subject under discussion, based on detailed clinical and personality studies of 50 cases, unselected except for the exclusion of thyrotoxicosis from the series. It was interesting that more than half of these were volunteers or territorials. These observers had found four main personality types. Two of these, roughly similar, had the rigid inner drive, were perfectionists and " obsessionals ", the third and fourth were an instinctually immature and physically inferior group, either of the over-compensating " Mother's boy " type, or else " quitters " from the start. These latter two were presumably the same as Dr. Lewis's psychopathic personalities.

Many had a long history of nervousness in pre-military life, and emotional stress formed the most important and constant factor in a complex ætiological picture, in which alleged " physical strain " was often in reality negligible. Major Dicks had himself seen a typical case who asked to be allowed to take exercise as his cardiac symptoms were worse in bed.

The speaker further pointed out how frequently phobic symptomatology was observed in *effort syndrome* patients. As regards psychopathology, the underlying mechanism was that commonly found in those with obsessional over-conscientiousness—fear of their own instincts, chiefly of aggression and of fear. They therefore readily seized on any temporary state of cardiac overactivity, breathlessness or debility (as after febrile illness) as an escape from these problems, and from the related situation of rebellion and subordination. In the other types, a more hysterical motive of escape from unpleasantness, and the " spoilt child " wish to be ill and dependent, provided the explanation.

Psychotherapy of the former group should be directed to loosening the grip of the rigid " super-ego ", and to foster release of aggression in healthy ways. It would then be found that so-called fatigue was frequently a state of inhibition of aggressive trends. He thought reductive and abreactive analytical techniques, e.g. under narcoanalysis (evipan, &c.), were most valuable. The inferiors and psychopaths, on the other hand, were best discharged as martial misfits.

He agreed that *effort syndrome* was but a somatic symptom picture common to a variety of psychoneurotic states, and not deserving of separate status.

Section of Medicine

President—Sir Maurice Cassidy, K.C.V.O., M.D.

[*April* 22, 1941]

DISCUSSION ON THE NATURE AND TREATMENT OF THE EFFORT SYNDROME

Dr. H. J. Starling: The history of this disability was set forth by R. McNeil Wilson in 1916. A Royal Commission sat from 1864-68 to investigate the nature and cause of this complaint. It was then defined "as an extreme sensibility of the heart with some but not great enlargement. During rest a heart of this kind beats easily, but on the least exertion its action becomes irregular and the man becomes breathless". The causation was ascribed largely to the type of accoutrements, and the principle of the brace was recommended to take the weight of the pack off the chest while the tunic at the same time was made looser. When one reads the history of the wars of those days, especially those fought in India with tight-fitting tunics, the weight of the accoutrements and sometimes of busbies, the diet and the drink, the temperature and the climate, and the extraordinary exertions demanded of the men, it is amazing that any of those hardy soldiers escaped a breakdown.

In 1864, Harthorne in the *American Journal of Medical Science* described *effort syndrome* during the Civil War, almost exactly as we know it to-day, anticipating Da Costa's classical work which appeared in the same journal in 1871.

In 1870 in this country, Arthur Myers published a treatise on "Diseases of the Heart among Soldiers" and emphasized the blame which had already been put on accoutrements and on the tight-fitting tunic. In 1876 Surgeon General Arthur Davy ascribed to the "setting up drill" an expansion of the chest, a dilatation of the heart and also irritability of its action. This view was again set forth in 1880 by Brigadier-Surgeon Veale and as late as 1896 by Surgeon Captain J. B. Wilson.

Until the conclusion of the Great War of 1914-18, the main interest in this disability had been aroused by the increase in its incidence during active warfare. This was certainly the case in America where during the Civil War the troops were badly clothed, badly fed, overtasked and generally neglected.

It was Thomas Lewis who, with the Staff of the Medical Research Committee, first defined the condition as *effort syndrome*, separated it from organic cardio-vascular disorder, and instituted the only way by which it could be alleviated or cured. It was an unforgettable experience seeing these men admitted to the Military Heart Hospital at Colchester, and subsequently recording the reaction of each man daily after the carefully graduated exercises from which they reported. One witnessed them at first sweating, distressed, generally tremulous and with varying high rates of pulse

and respiration, often "done to the world", but lastly able to stand the test of the highest grade of drill.

At least 50%, probably 70% of the civilian population when taken from their secluded, or at least peaceful, routine of life are liable to *effort syndrome*. Many of these already suffer from it in various degrees, but, in spite of this, manage to fulfil their daily work in their particular niche without obviously breaking down. Even the most stable members of the population under certain conditions may develop this disability.

Among the mass of patients at Colchester were a few outstanding men who appeared quite normal. They had no tremor, no distress, but only dyspnœa and tachycardia on effort. Almost invariably they were found to have some form of organic heart lesion. Yet in most cases they had not experienced any greater effort or strain than they were accustomed to in civil life.

Lewis, in discussing the ætiology of *effort syndrome*, writes: "The psychology of our patients as a group is not that of the average soldier; a large proportion of the men are of highly strung nervous temperament; an unusual number are sensitive or querulous, others are apathetic or depressed." The whole atmosphere was one of re-assurance and encouragement, combined with re-education in the lost faculty of effort without distress. The proof that Lewis's measures were the right ones was shown in the large proportion of men who were fitted to return either to front line or home-service duty, and also by the dogged courage with which, while the war was on, the men stuck to their daily exercises and their cure.

Professor F. R. Fraser (*Edinburgh M. J.*, 1940, **47**, 451) on *Effort Syndrome*, quotes a personal communication from Dr. Paul Wood wherein it is stated: "War service, whether at the front or behind the lines, or even in England, has brought on the symptoms or has exaggerated them. On the whole the 'patient' does not like war service and is disposed to get out of the Army if he can. He is therefore prepared to make the most of his symptoms and is not averse to any term which connects his heart with his disease as he feels such a term is honorable and a potential source of sympathy. In civilian practice one is familiar with the pleasure with which most people are reassured about their hearts and it is interesting to watch in its place the concern that some of these men depict when they are told that they have no such refuge."

As Chairman of a Medical Board I see about 300 men every week. There is an immense improvement in the young men of 18 to about 26, in their health and good physical and muscular development. They are keen to enlist, whether as volunteers or under the National Service Act. I have been immensely impressed with the real beauty of the majority of these youths both in features and in appearance. It is interesting to note that a Board consisting entirely of volunteer enlistments or a Board of those under the National Service Act who have plumped for the Air Force is invariably of a finer type than any other category of Boards. Later, when statistics are available, I shall be anxious to see if these types of young men, especially the volunteers, constitute any large proportion of the *effort syndrome* cases, and if the statistics could show what district these men came from and by which Board they were examined, in order, while there is yet time, that methods and assessments might be revised.

I am doubtful about the value of the exercise tolerance test during a medical examination. Young men, many of whom are anxious to be in the first grade, arrive with pulse-rates of 100-120; the 20 times chair test may increase the pulse-rate to 140-160, as a rule without any dyspnœa, and after a minute the pulse returns to its original high figure, perhaps higher. I make it my duty to ascertain what games they play, if football, then in what part of the field, if hiking, for what distance; some of the highest figures have occurred among the most athletic, including both short and long distance runners as well as swimmers, and in lads accustomed to heavy work. This test is of value if it occasions actual distress or dyspnœa, but details as to capacity for effort in the recent past together with an estimate of the candidate's "make up" generally are of more importance.

The real national problem of this disability is not so much the cure or alleviation of the cases which arise as the result of the war, but the means whereby it may be prevented before any war starts.

The worst type of *effort syndrome* is seen in the lad who is often subject to minor infections, is diffident, keeps himself to himself and never makes friends, and so leads

a solitary existence wrapped up in his own world; he is moreover often spoilt by an indulgent and over-anxious mother. Most of us have traits like these to a greater or less extent. Public school life, with its almost compulsory games, is one of the best cures for the curable, added to which the life at school is a definite release from the anxious atmosphere of home life.

Psychiatry may be of enormous value in bringing the nervous, solitary or anxious type to a more normal aspect of life so as to fit these individuals to mix and compete with their fellows and to take every advantage of such physical training as comes their way. But in time of war its use should be devoted chiefly to those who do not respond to simple encouragement, reassurance, and graduated exercises, and it certainly cannot be used except in its most elementary form during the examination by Medical Boards.

The observation of Parkinson and others that *effort syndrome* is not common in the Navy is important. This may be accounted for largely by the refusal to accept for active naval service any grade below the first. Similarly I well remember seeing a rare case of *effort syndrome,* a man who had been in a Guards regiment. He looked as if all the struts had been removed from his once magnificent chest, the contents of which appeared to have dropped into his sagging abdomen. The chest expansion by measurement was as good as before, but the posture of the man had completely changed. In the Guards, as in the Navy, the physique of a recruit must be first-class and both these Services are exposed to hardships and terrifying experiences. This seems to show that a member of these specially selected Services, possessing a fine physique, is only in rare instances liable to the disability we are discussing. The antecedents of such men postulate a record of good family life, sound spiritual upbringing and family tradition, all of which are fast disappearing from our national life.

I would advocate for at least one year, preferably two years, a communal outdoor life for our lads. This should be devoted for the first six months to games, physical drill, and general education at the age of 17 or 18, and for the rest of the time to military education, not forgetting its historical aspect. Let us hope that these lads will not be wanted for active warfare, but there is no doubt that such training will enormously enhance their national value in civil life.

Dr. Paul Wood: *Differential diagnosis of Da Costa's syndrome.*

In introducing the name "Da Costa's syndrome" I wish to make it clear that I do not propose its use as a diagnostic term to replace *effort syndrome.* As I have said elsewhere (*B. M. J.*, 1941 (i), 850) I believe the facts show that the condition always results from emotional causes, which may operate in almost any form of psychoneurosis. Thus we are asked to discuss a syndrome which is really a psychosomatic pattern, not a distinct clinical entity. To call this *effort syndrome* is to evade the etiological diagnosis, and to emphasize what is least important. Believing that the old conception will die, I have thought it fitting that it should bear an historical name. Thus Da Costa's syndrome describes without prejudice a certain psychosomatic pattern, and implies an historical attitude towards it. A review of the American and English literature from 1858-1941, close personal contact with some 300 patients, and certain researches, have led me to conclusions about the nature of this syndrome which will be published in due course (*Brit. M. J.*, 1941 (i), 767, 805, 843).

It has been the custom to diagnose Da Costa's syndrome by eliminating organic disease. Yet the family history reveals neurosis in over 50%, compared with 7% in 125 controls; the life story of the patient is diagnostic in about 75%; there are some 20 characteristic symptoms, the majority of which are present in any given case; and there are some 15 typical signs (*vide* Table I). Da Costa's syndrome is therefore a positive diagnosis, not a negative one. However, it is often mistaken for a weak, tired, or strained heart, for rheumatic or toxic carditis, "V.D.H.", anæmia, thyrotoxicosis, pulmonary tuberculosis, pleurisy, influenza, angina pectoris, or malingering.

It cannot too often be repeated that terms such as weak, tired, or strained heart, are just nonsense, and that their continued use is harmful. Whether they are used carelessly or in ignorance is irrelevant, their effect is the same, and may be responsible for total incapacity. Anæmia, pulmonary tuberculosis, pleurisy, and influenza, should present no difficulties with reasonable care, and the difference between left infra-

mammary pain and angina pectoris has been recited again and again. My observations concern the remainder.

TABLE I.—SYMPTOMS AND SIGNS IN 200 CASES OF DA COSTA'S SYNDROME.

System	Symptom	Per cent.	Sign	Per cent.
General	(1) Fatigue	88	(1) Typical facies	31
	(2) Nervousness	79	(2) Nervous manner	48
Vasomotor	(3) Palpitations	89	(3) Overacting of heart or great vessels	44
	(4) Vascular throbbing	57	(4) Tachycardia	
			Pulse > 90 at rest	28
			Pulse > 100 standing	35
	(5) Dizziness	78·5	(5) Blood-pressure > 150/90	27
	(6) Headaches	72·5	(6) Deceleration time longer than 2 mins.	33
	(7) Syncope	34·5	(7) Cold blue hands	44·5
	(8) Paræsthesia	56	(8) Visible flushes	36·5
	(9) Flushes	57		
Respiratory	(10) Breathlessness	93	(9) Hyperpnœa or tachypnœa	21·5
	(11) Sighs—inability to obtain satisfying breath	62	(10) Frequent sighs	32
			(11) Breath-holding time less than 30 secs.	76
Sudomotor	(12) Undue sweating	80	(12) Palmar sweating (visible)	67
			(12) Axillary sweating (trickling)	35
Muscular and skeletal	(13) Trembling and shakiness	65	(13) Tremor or shakiness	26·5
	(14) Cramps	57	(14) Poor development	+
	(15) Left thoracic pain	78	(14) Asthenic posture	41
			(15) Hyperalgesia over area of pain	+
Gastro-intestinal	(16) Dry mouth	55		
	(17) Anorexia	20		
	(18) Vomiting or diarrhœa	26		
Other	(19) Insomnia	18·5		
	(20) Frequency of micturition	10·5		
	Phobias and nightmares	+		

Rheumatic carditis.—It is rightly held that failure to diagnose rheumatic carditis is a serious mistake; but to diagnose rheumatic carditis when the heart is innocent is often more serious. It must be borne in mind that neurotic subjects often develop somatic manifestations during childhood, and often complain of vague pains which are too readily labelled rheumatic. The fatal error is to note the tachycardia and the "rheumatism" and to miss the nervousness. Even if a patient has true rheumatic fever it does not follow that the heart is involved; and even if it is, there is no need to turn the patient into a cardiac invalid.

In the hope of clarifying the significance of the signs upon which the diagnosis of rheumatic carditis is often made, I have presented them under four headings in Table II. Many of them merely indicate disturbance of the autonomic nervous system from any cause; others are signs of infection, but are non-specific; a few mean that the infection is rheumatic; some are true signs of rheumatic carditis. The items in the first column may all be produced by emotional stimulation, and indeed commonly are; if there is evidence of non-specific infection, there is no justification for diagnosing rheumatic fever, whether there is a systolic murmur and tachycardia or not; of the signs in the third column chorea alone is followed by mitral stenosis in only 20% of cases

(Sutton and Dodge, 1938), whereas rheumatic nodules in a child signify such a degree of infection as to make carditis practically certain; any one of the signs in the fourth column justifies a cardiac diagnosis.

TABLE II.—SIGNIFICANCE OF CERTAIN SIGNS RELATING TO DIAGNOSIS OF RHEUMATIC CARDITIS.

Disturbance of the autonomic nervous system (non-specific)	Evidence of infection (non-specific)	Specific rheumatic infection	Rheumatic carditis
General malaise	Fever	Joint pains	Transient mitral diastolic murmur
Facial pallor	Raised sleeping pulse-rate	Polyarthritis	Development of aortic incompetence
Anorexia	Leucocytosis	Chorea	Pericardial friction or effusion
Loss of weight	Accelerated blood sedimentation rate	Rheumatic nodules	Presystolic gallop
Fatigue	" Secondary " anæmia	Erythema marginatum	Congestive failure
Sweats	Erythema nodosum		X-ray evidence of cardiac enlargement
Palpitations			Partial heart block
Tachycardia			Other electrocardiographic evidence
Overaction of heart			
Breathlessness			
Odd pains			
Faintness			
Syncope			

It must happen that a child may have rheumatic carditis without the evidence required, for 30 to 40% of patients with mitral stenosis give no rheumatic history. There is no evidence that these mild cases suffer from want of rest in bed at the time.

Toxic myocarditis.—In a modern textbook of cardiology (Cowan and Ritchie, 1935), the following passage is written with reference to " D.A.H.": " Acute febrile illnesses always produce changes in the myocardium. . . . inflammatory reactions leave scars which, although minute, may from their ubiquity interfere gravely with the cardiac strength. In many cases an apparently trivial illness, such as influenza, may hit the heart heavily, especially if the patient carries on throughout the acute stage of the disease, exposing the weakened heart to the stress and strain of physical exertion." This clearly expresses the view that post-infective cases of Da Costa's syndrome are due to a cardiac fault, and Wiggers (1923) and MacKenzie (1916) have recorded similar views.

Proof of the validity of these statements is lacking. On the other hand there is good evidence that toxic carditis occurring during acute infections such as diphtheria and pneumonia are always transient, and leave no scars to interfere gravely or otherwise with the cardiac strength. Wolbach and Frothingham (1923) paid special attention to muscle damage in an autopsy study of 26 cases of influenza, and found that the heart escaped demonstrable injury, although the rectus abdominis showed necrotic hæmorrhagic lesions in nine. During the influenza epidemic of 1936-37, I examined a number of severe cases with Drs. Stuart-Harris and Scadding, and took electrocardiograms of any who had symptoms which might have been due to the heart, but no evidence of carditis could be discovered by clinical or laboratory methods, nor have I at any other time found such evidence. At the Emergency Hospital influenza was an apparent causative factor in 17% of my series, but clinical, X-ray, and electrocardiographic examinations revealed no signs of carditis.

I do not, therefore, believe that Da Costa's syndrome has to be distinguished from toxic carditis, because there is no evidence that toxic carditis outlasts the infection which produces it, whereas there is good evidence to the contrary.

V.D.H.—It is often said that the symptoms of *effort syndrome* are indistinguishable from those of early organic heart disease, and that on the history it is impossible to say that the case is not one of mitral stenosis. During the past year I have examined 100 recruits with early organic heart disease, 80 rheumatic cases with various combinations of mitral and aortic valve disease, 18 congenital, and 2 cases of rhythm changes. Symptoms occurred in 21, and in 13 of these the characteristic features of Da Costa's syndrome were present. The lack of relationship between the symptoms

and the size of the heart (Table III) supported the view that they were not usually of cardiac origin. Only 8% had symptoms which seemed to be referable to the heart itself. The remaining 79 cases were symptomless, and 59 of them were known to be capable of exerting themselves to the full without distress. It is concluded that inactive early organic heart disease rarely produces symptoms, and should not, therefore, be confused with Da Costa's syndrome.

TABLE III.—RELATIONSHIP OF SYMPTOMS TO THE SIZE OF THE HEART IN CONSCRIPTS WITH UNCOMPLICATED ORGANIC HEART DISEASE.

Degree of cardiac enlargement (as judged on X-ray screen)	No. of cases	Symptoms			
		None	Like those of Da Costa's syndrome	Probably cardiac	Total with symptoms
None	32	24	7	1	8
Slight	39	31	3	5	8
Moderate	23	20	2	1	3
Considerable	6	4	1	1	2

Systolic murmurs are still a source of confusion. To dismiss them as functional, without offering any explanation as to their origin, is to prolong this confusion, for it is the lack of understanding of the systolic murmur which is partly to blame.

Experiments made by Ortiz (1939) proved that soft blowing murmurs could be reproduced by friction between two normal endothelial surfaces normally lubricated. This may explain some of the murmurs of overacting hearts, where such friction is increased.

Slight mechanical interference with the expansile pulsation of a large vessel, such as the common carotid artery, may produce a murmur and thrill, a fact which may be readily checked by placing the finger on such an artery and exerting gentle pressure. The more overacting the artery, the more easily is the murmur or thrill produced. When the heart is overacting, the pulmonary artery may come into firm contact with the chest wall, especially in thin subjects with flat chests, and the pressure exerted upon it during its expansile phase may well give rise to a systolic murmur, if not to a thrill.

The respiratory murmur is more generally recognized. It is due to sudden squeezing of lung tissue between the heart and chest wall, or to sudden expansion of a portion of lung which was compressed by the heart during diastole; it varies with respiration and with change of posture, and is more likely to occur when the heart is overacting.

The fourth mechanism for the production of an innocent systolic murmur depends upon the fact that the mitral valve is only competent so long as the mitral ring constricts adequately during ventricular systole. This mechanism may be faulty, even in normal persons. The effect of such a leak on cardiac function is negligible.

Systolic murmurs may, however, represent organic mitral incompetence. I have investigated this subject at some length, but details will have to be published elsewhere. The diagnosis rests upon the presence of at least three of the following features:

(1) Previous rheumatic infection.

(2) An impressive mitral systolic bruit, with or without thrill.

(3) X-ray evidence of left ventricular enlargement.

(4) Electrocardiographic evidence of left ventricular dominance.

(5) X-ray evidence of expansile pulsation of the left auricle during ventricular systole, best recorded with the kymograph.

Early hypertensive heart disease.—Da Costa suggested that hypertrophy eventually followed the overaction of the heart so often witnessed in these men, and Osler (1901) seems to have regarded the syndrome as due to early hypertensive heart disease. Because the blood-pressure, both systolic and diastolic, is apt to be raised during casual examination, and because I have often been asked whether this signifies early hypertension, I have thought it pertinent to give the evidence which shows that it does not.

Hines (1940) has shown that incipient, early, and late hypertensives react unduly to the cold pressor test, which consists of plunging the hand and wrist into water at 4° C. and keeping it there for one minute, while the blood-pressure is recorded in the other arm. In hypertensive subjects the systolic blood-pressure rises more than 20 mm. of mercury, and the diastolic more than 15. Similar positive reactions occur in 15% of controls—regarded by Hines as potential hypertensives. The average rise in the remaining 85% of controls is 12·4 for the systolic, and 10·1 for the diastolic pressure. Using the technique and precautions described by Hines, I found that 10% of 25 cases of Da Costa's syndrome gave a positive reaction, and that the average rise in the other 90% was 8 mm. of mercury for the systolic pressure, and 8·5 for the diastolic. It is concluded that these are not cases of early or incipient hypertension.

Better evidence was afforded by the follow-up studies of Grant (1925). He kept in touch with 601 cases over a five-year period, and of these only 1% developed heart disease.

Other forms of heart disease.—There are still those who believe that some queer form of heart disease may actually be responsible for some cases of Da Costa's syndrome. These physicians may refer to left infra-mammary pain as being "a true bill" when it occurs in this hypothetical group. This loop-hole is highly dangerous, and will prolong false cardiac diagnosis unless closed. The proof that the heart is innocent is as follows:

(1) Congestive heart failure has never been recorded.

(2) Left infra-mammary pain is produced locally, in the muscles, fibrous tissue, or fascia of the thoracic wall, and is not referred from the heart (Wood, 1941). It is never a "true bill" in the cardiac sense.

(3) Cardiac enlargement has never been seen on X-ray examination (Craig and White, 1934). I have screened about 500 cases of *effort syndrome* in hospital, and in private practice, and have encountered no instance of enlargement in the absence of known forms of organic heart disease. Bass and Wessler (1913) found the heart smaller than usual in 22 out of 36 cases of *effort syndrome* in children. This was confirmed by Friedländer and Freyhof (1918) in 50 constitutional cases, and by Meakins and Gunson (1918); Smith (1920) found that the average transverse diameter of the heart in 119 cases of *effort syndrome* was 0·98 cm. less than that in 277 controls; that when comparisons were made between patients and soldiers of the same weight, the volume of the heart averaged 10·1% less in the patients than in the normal soldiers; and that these small hearts were found in the constitutional type of *effort syndrome*, not in the acquired. It is probable that the small heart, when present, is the result rather than the cause of the condition; for it is the reverse of what is found in the athlete after long training (Parkinson, 1936), in cases of bradycardia of long standing (Schlomka and Broich, 1937), in very active animals, e.g. hares (Herrmann, 1926), and in animals after long periods of strenuous exercise (White, 1937, page 394).

(4) The electrocardiogram is normal in the great majority of patients, and was first shown to be so by Parkinson and Drury (1916) who also showed that it remained normal after effort. Very occasionally, inversion of the T wave may be found in leads 2 and 3 (Graybiel and White, 1935). It has been normal in all but 1 of 50 cases in which I have taken it, the exception showing inversion of the T wave in leads 2 and 3. The explanation of these rare graphs may be found in a recent article by Mainzer and Krause (1940), who showed that they could be produced by the anxiety of lying on an operating table prior to the anæsthetic.

(5) Follow-up studies of 601 patients over a five-year period (Grant, 1925) revealed that only 1% developed clear signs of organic heart disease, a figure no higher than controls.

(6) If Da Costa's syndrome were due to some unknown form of organic heart disease, it would be the only kind which has never been known to produce death. It is, of course, for this reason that autopsy studies are so scarce.

(7) When recovery occurs it may take place suddenly, almost abruptly (*see* Lecture 3, *Brit. M. J.* (i), p. 848).

Thyrotoxicosis.—The idea that thyrotoxicosis was the cause of *effort syndrome*, put forward by Sir James Barr (1916), and supported by Brooks (1918), and in part by Swan

(1921), has been adequately quashed by numerous authors, including Friedländer and Freyhof (1918), Addis and Kerr (1919), Kessel and Hyman (1923), and Martin (1939). Differential diagnosis, however, still appears to present difficulties. Thus Kessel and Hyman were unable to express the clinical difference in words ; Lambert Rogers (1941) offers us four points of difference, and yet two of these (good appetite and positive adrenaline test) are often found in Da Costa's syndrome as well as in thyrotoxicosis ; and only the other day I heard the view expressed in a London teaching hospital that the basal metabolic rate was the only distinguishing feature. It may therefore be worth while to set out these differences in full.

(1) In an attempt to express what Kessel and Hyman noted but failed to describe, I would say that thyrotoxic patients tend to deny that they are ill, they have a ready excuse for their symptoms, are anxious to get out of hospital and return to work, fight the restrictions imposed upon them, and are inclined to view their physician as an enemy. Patients with Da Costa's syndrome present a striking contrast ; they are only too ready to agree that they are ill, they produce symptom after symptom challenging the physician to explain them, they are prepared to lie in bed indefinitely, and they seem to welcome restrictions. Appearances are equally distinctive. In thyrotoxicosis the eyes not only stare but gleam ; the expression is alert, the manner abrupt, the mood aggressive, the whole effect hyper-kinetic. In Da Costa's syndrome the eyes are dull, the expression worried, the manner timid and often slow, the mood depressed—the whole attitude suggesting failure, despondency, and inactivity.

(2) Examination of the hands is especially fruitful. In thyrotoxicosis they are warm, pink, and moist on the back as well as on the palm, and tremor is fine and regular ; in Da Costa's syndrome they are cold, blue and moist on the palm but not on the back, and the tremor is coarse, irregular, and inconstant.

(3) Goitre is no more common in Da Costa's syndrome than in controls (Addis and Kerr, 1919).

(4) The sleeping pulse-rate is normal in Da Costa's syndrome; it averaged 60-65 in Hume's series (1918). So is the basal blood-pressure which averaged 121/73 in McCullagh's series (1934), and 117/75 in Cohn's (1919).

(5) The basal metabolic rate may not be easy to measure, on account of the irregularity of the tracing in those with respiratory neurosis, or because of the difficulty in obtaining basal conditions in nervous subjects. True readings, however, are normal (Peabody, Wearn and Tompkins, 1918).

(6) Iodine lowers the pulse-rate, increases the body-weight, reduces the nervousness, increases the size and tension of the thyroid gland, and generally improves the thyrotoxic patient in the well-known manner ; in Da Costa's syndrome it does none of these things.

In the E.S. Unit I have not seen a single case which looked like thyrotoxicosis, and not once have I found it necessary to ask for a basal metabolic rate. Indeed we have never even used the iodine test.

Malingering.—By a malingerer I mean a man who says he has symptoms when he knows he has not.

The objective signs of autonomic disturbance set out in Table I make the gamble of the malingerer risky. Two-thirds of the patients have five or more of these signs, and 87% have three or more, compared with 2% in 50 controls. Thus a soldier may concoct the whole story of *effort syndrome* but if his autonomic nervous system remains undisturbed, he is at once suspect, and needs careful cross examination. Not that it is easy to make up the involved and highly characteristic history of these patients—far from it. The symptoms too are not so easily thought of (cf. pain in the back) ; as Allbutt said (1917): "This group of symptoms is too uniform to be fictitious or fantastic."

However, I have no doubt that exaggeration is the rule. It is the common object of these men to improve their lot, and they are not faddy as to how they do it. The best instructors in the use of the symptom weapon, especially the cardiac variety, are medical officers.

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Dr. Aubrey Lewis said that the term *effort syndrome* was not synonymous with *anxiety neurosis* as it included many other psychiatric conditions. Some patients with *effort syndrome* suffered from depression or hysteria ; others had a psychopathic personality ; there might also be a few schizophrenics or alcoholics among them. Therefore a uniform plan of treatment for all cases could not be successful.

Effort syndrome meant a physiological as well as a psychological disturbance, although, as a group, these men were not physically inferior.

Dr. Lewis went on to say that the problem of *effort syndrome* was at once individual and social. Not only must the sick man himself be carefully studied, but his milieu, privations and discomforts in contrast to his former life must all be considered.

Dr. Maxwell S. Jones, and Dr. Ronald Scarisbrick : *A Comparison of the respiration in patients with* effort syndrome *and in normal subjects.*

Breathlessness ranks with palpitation and precordial pain as the commonest complaint in *effort syndrome*. During the course of a routine examination on subjects with *effort syndrome* but little information is usually obtained, apart from evidence of an overacting heart, and even after moderately severe exercise the objective picture may not indicate the degree of distress which the patient subjectively describes. It therefore seemed desirable to obtain further objective evidence of the patient's disability. The familiar exercise tolerance test, in which the subject climbs 30 steps in approximately 30 seconds is an attempt to measure the response of the heart-rate to exercise, with particular reference to the deceleration time. As an isolated observation this has little or no value, but in the total assessment

of a case it may be helpful. In any case, however, disturbance of cardiac function is frequently indicated, even at rest, by a rapid heart-rate and a visible apex beat.

Less obvious is objective evidence of disturbance of function in the respiratory system, although the patient's subjective account almost invariably describes breathlessness on mild exertion, on excitement, or at rest. Patients also describe choking sensations when they waken suddenly at night, and lie gasping for breath, for some minutes. Difficulty in wearing a gas mask for more than a few minutes because of feelings of suffocation is also very common, as is also the desire to sigh frequently.

It seemed necessary to study the respiratory style in these men and if possible to try and evolve a test of respiratory efficiency which would demonstrate any deviation from normal respiration, particularly following exercise. Tests of respiratory efficiency have been conveniently summarized by Moncrieff (1934), who points out their limitations and concludes that as yet there is no one test which can be regarded as satisfactory.

Method.—The form which our respiratory exercise tolerance test took was as follows: The patient lay on a couch and breathed into a spirometer filled with oxygen; the Benedict (Kendrick) portable metabolism apparatus was used. No attempt was made to achieve "basal" conditions but freedom from anxiety and familiarity with the procedure was aimed at. After a trial run which, in the majority of subjects, had been done on a previous day, the kymograph was started and the respirations recorded for a period of 4 to 5 minutes. The apparatus was then disconnected and the spirometer bell refilled with oxygen. The patient now ran up and down three wooden steps, each 8 in. high, ten times, in approximately 30 seconds. He then lay down immediately, and was connected up with the spirometer: the time relationships required for these various steps were recorded on the tracing simply by tapping the spirometer bell at the appropriate moment.

It was found that the procedure was less unpleasant for the subject and consequently better tracings obtained, if the closed circuit was broken every 2 minutes by turning the tap so that the outside air was freely breathed in and out: after 1 minute the tap was again closed so that the subject breathed into the spirometer. Thus the final tracing recorded breathing at rest for 4 to 5 minutes, the time required for the exercise, the time lost between the completion of the exercise and breathing into the spirometer circuit, and the breathing 1 to 2, 4 to 5, 7 to 8, and 10 to 11 minutes after exercise. At the completion of the test, or on a separate occasion, the vital capacity was measured together with the length of time the breath could be held, starting at the top of a normal inspiration following a period of rest.

Results

32 patients free from apparent organic disease and conforming with the diagnosis of *effort syndrome*, together with 22 normal controls, all male, were examined. Striking differences between the two groups were apparent in the respiratory style, the average volume per breath, the respiratory rate, the breath-holding, the return of the minute volume to the resting level after exercise, and to a lesser extent the vital capacity.

The respiratory style was remarkable, particularly because of the irregularity of the breathing, this irregularity being more noticeable in depth than in time. In only seven patients were the expiration points so regular that they collectively formed a straight line, i.e. no measure of oxygen uptake was possible in the majority of patients. By comparison, the controls showed regular breathing in almost every case, and indeed in ordinary clinical work it is seldom that one has to discard a spirogram tracing because it is too irregular for the purpose of calculating the B.M.R.

The depth of the breathing was very different in the two groups. In the controls the average volume per breath at rest was 910 c.c. (Table I). In the *effort syndrome* patients the average volume per breath was 520 c.c., the patient with the shallowest breathing having an average volume per breath of 407 c.c. It must be remembered that the lungs contained a high percentage of oxygen which increases the tidal air by 13%.

The patients with *effort syndrome* breathed, on the whole, much more rapidly than the controls, the average rate at rest for the two groups being respectively 20·5 and 11·7 breaths per minute.

TABLE I.—MEAN VALUE OF RESPIRATORY DATA FOR A GROUP OF 22 CONTROL SUBJECTS AND A GROUP OF 32 EFFORT SYNDROME PATIENTS BEFORE AND AFTER EXERCISE.

		Time after exercise (minutes)							
	Rest	1	2	4	5	7	8	10	11
Control Group.									
Minute volume (litres)	10·7	20·5	14·7	12·4	12·0	10·5	10·5	9·2	9·7
Minute volume as percentage of resting value	100	191	146	118	114	99	97	88	90
Respiration rate	11·7	12·6		11·9		11·8		11·2	
Volume per breath (c.c.) . .	910	1,400		1,060		940		810	
Effort Syndrome Group.									
Minute volume (litres)	10·6	27·4	22·5	17·4	17·0	13·8	12·9	11·1	11·0
Minute volume as percentage of resting value	100	256	209	160	156	124	120	103	111
Respiration rate	20·5	27·9		24·0		22·4		21·1	
Volume per breath (c.c.) . .	520	940		700		610		500	

Breath-holding was done extremely badly by the patients, the range being from 6 to 54 seconds with a mean of 18·4 seconds. The controls gave a range of 24 to 212 seconds, with a mean of 72·0 seconds.

Vital capacity measurements undertaken with the subject lying down showed a range of 1,600 to 5,300 c.c. with a mean of 2,840 c.c. in the *effort syndrome* patients, while the controls showed a range of 2,800 to 5,500 c.c. with a mean of 4,172 c.c.

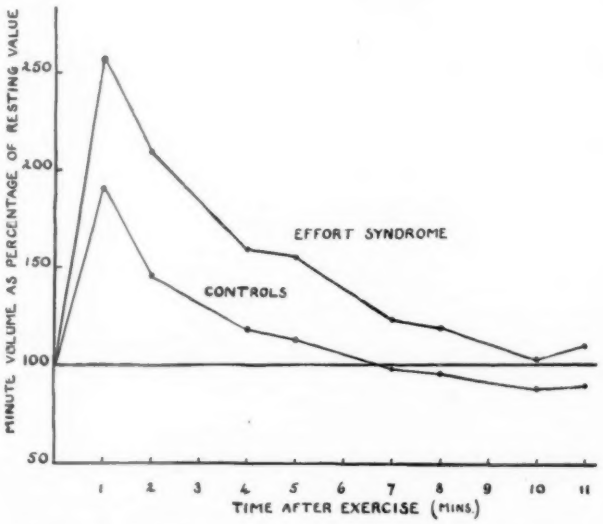

FIG. 1.—Percentage increase of minute volume after exercise.

However, the point which we regard as being the main value of spirography in this field, is what we call the respiratory exercise tolerance test. By this we mean the alteration in the minute volume of respiration as a result of exercise and the time of its return to the resting value. In Table I is shown the minute volume of the controls as a group, and of the *effort syndrome* cases as a group, at rest, and at the various periods following the exercise. The minute volume after exercise has also been expressed as a percentage of

the resting value and this is plotted as the ordinate in fig. 1, the abscissa represents the time after exercise at which the minute volumes were recorded. Fig. 1 shows clearly the difference in the respiratory response to exercise of the *effort syndrome* patients and the control group. The rise in the volume of respiration which follows exercise is much greater in the *effort syndrome* patients than in the controls and takes considerably longer to return to the resting value. The difference is, perhaps, most obvious in the fourth and fifth minutes after exercise, when the control group is within 20% of the resting value, whereas the *effort syndrome* patients still showed a 60% increased respiration. Most of the really fit people amongst the controls showed a respiration almost back to normal at this point.

The minute volume of respiration is far from an ideal measure of respiratory function. It gives no real indication of the subjective respiratory difficulty or of the actual effort made as compared with the maximum possible respiratory effort. The latter is partly conditioned by the vital capacity and as this is relatively small in *effort syndrome* and the minute volume after exercise relatively large, severe respiratory difficulty may ensue. By way of illustration, the average minute volume for the minute immediately following exercise is 20·5 litres for the control group and 27·4 litres for the *effort syndrome* patients, while the average vital capacities found for the two groups are 4·17 and 2·84 litres respectively. Thus the control group use, as it were, their vital capacity 4·8 times and the *effort syndrome* patients 9·8 times in one minute. Furthermore, the minute volume does not give a direct indication of the actual air exchange in the lungs, for with every inspiration a proportion of the previously expired air is returned to the lungs. The more rapid the breathing, the more does this dead air space reduce the actual ventilation. As a result of this, the actual ventilation of the *effort syndrome* group at rest is below that of the control group. The proportional increase in actual ventilation as a result of exercise is greater than the proportional increase in the measured respiration; this applies to both groups but is more marked in *effort syndrome*.

It must again be emphasized that these experiments were carried out with a high partial pressure of oxygen in the lungs and it is to be expected that the performance of the test in air would show greater deviation of respiration from the resting level.

Summary.—The *effort syndrome* patients used for these tests were not specially chosen; the only criterion was a symptomatic one, i.e. all the patients had the characteristic symptoms of *effort syndrome*. This means that viewed psychiatrically the patients were a mixed group of anxiety states, depressions, hysterics, and post-infective states.

Haldane and his collaborators (1919) working on the problem of *effort syndrome* during the last war, laid great stress on what they regarded as the characteristic rapid shallow breathing of this condition. They considered this type of breathing, brought about by an exaggerated Hering-Breuer reflex produced by irritation of the lungs during gassing, or as the result of a hypersensitive nervous system, led to anoxemia which depressed the respiratory centre and resulted in the setting up of a vicious circle. It may be that they were dealing with a particular respiratory group, or that patients who had been previously gassed formed a large percentage of their cases, for our experience here has been different. Of the last 100 admissions to the *effort syndrome* unit at this hospital, only five had average resting respiratory rates of over 35 per minute. Certainly in the group studied here the rate of respiration at rest was fast, 20·5 respirations per minute (approximately twice as fast as the controls) and the average volume per breath was low (520 c.c.) as compared with the controls (910 c.c.). These figures are different from the figures quoted by Haldane and collaborators who, in an unstated number of cases, invariably found rapid shallow breathing of 20 to 60 or more respirations per minute with an average volume per breath of 250 to 350 c.c. They found that the rate increased abnormally after exercise, while the increase in depth was small. In the patients here presented the rate of respiration after exercise rose from 20·5 to 27·9 per minute during the first minute after exercise, while in contra-distinction to Haldane's patients the average volume per breath rose from 520 c.c. to 940 c.c.

Soley and Shock (1938), however, proposed that *effort syndrome* resulted from a washing-out from the blood of carbon dioxide by hyperventilation. In the group of *effort syndrome* patients studied, the amount of air expired at rest is approximately the same as in the control group. When allowance is made for the dead space, which is a

greater factor in the *effort syndrome* patients owing to their faster rate of respiration, the actual air exchange of the *effort syndrome* patients is less than that of the control group. We have had, however, two cases of spontaneous hyperventilation tetany and among the present series were two cases, both hysterics, in whom hyperpnœa was readily produced by an emotional state, who normally showed a respiration rate of 20 per minute. After exercise the ventilation of the *effort syndrome* group is greatly increased as compared with normals, but this does not necessarily mean that CO_2 is washed out of the blood—in the two hysterics mentioned the ventilation after exercise reached 57 and 38 litres per minute respectively without the production of any tetanic symptoms.

At first sight the views of Haldane and of Soley and Shock appear to be entirely opposed; this, however, is not necessarily true. Haldane was concerned solely with oxygen and Soley and Shock with CO_2. The ordinary spirometer gives no indication of CO_2 output and the tracings of the patients were too irregular to permit any accurate estimations of oxygen uptake being made. The impression gained in the present work is that the oxygen uptake immediately after exercise is more rapid in the controls than in the patients, but more accurate studies using the Douglas bag technique are now in progress.

There does not appear to be any obvious explanation for the relatively poor vital capacity and breath-holding capacity in these patients: we have found that breathing exercises did not lead to any marked improvement. Indeed, any "treatment" directed specifically towards the respiratory anomaly, e.g. attempts at slowing a very rapid rate by explanation, re-education, persuasion or suggestion have proved disappointing.

Clinically the respiratory exercise tolerance test would appear to be a useful objective measure of breathlessness after exercise, and even of physical fitness: those patients who have shown the quickest return to the resting minute volume after exercise have certainly done best at the P.T. class and conversely, a poor response would appear to indicate that the patient will do badly when given strenuous work. We are not yet ready to express any final opinion as to the value of this test; that it may be quite sensitive, however, is suggested by the fact that one of the controls who was suffering from post-tonsillitis asthenia, showed a marked improvement in the rate of return of the minute volume to the resting level, and of the O_2 consumption to the resting value, after two weeks' hard physical training.

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Colonel H. L. Tidy: In the last war, *effort syndrome*, the condition then known as D.A.H., became extremely important. It was believed that the element of fear was the main causative factor although it was noticed that a large proportion of the cases had only been two months in France. In the present war the main elements causing fear in the last war have not yet occurred. At present *effort syndrome* is a relatively trivial concern. In this country only about 200 beds are allotted to cases of *effort syndrome* and these include all the Services and the beds are not all occupied. After Dunkirk the majority of the cases recovered very rapidly. The results of hospital treatment are not fully known. At the end of the last war about 50% of the cases were sent back to the front line but it was not known what happened to them. A number of cases which have been treated in hospital in this war have relapsed subsequently and been admitted to hospital again It is not good policy to keep these cases in hospital until they are cured, that is to say, until they are temporarily free of all symptoms. Directly such men feel any symptoms returning they want to be cured again, that is, to be sent to hospital again. Getting them back to their units as rapidly as possible without waiting for a complete cure is the best method. Medical Officers of units should not be encouraged to send all cases showing any symptoms of *effort syndrome* to be admitted to hospital or even to see specialists as out-patients. Many medical officers have succeeded in getting such men through without sending them either to specialists or to hospital and there is no doubt that many men so treated become acclimatized and are subsequently useful soldiers.

A large number of men developing *effort syndrome* are below the physical average and their physical condition is not improved to any great extent in hospital. From the physical aspect they do better in the units. The term *effort syndrome* is not ideal, but any term which is used would acquire the same significance. Of course, the soldier is not supposed to see his diagnosis, but, in fact, he always knows it. It is better not to call the soldier's attention to his having any syndrome. When the symptoms have followed an infection, he should be regarded as convalescent from that infection and so diagnosed.

Clinical Section

President—G. DE BEC TURTLE, M.D.

[*March* 21, 1941]

MEETING HELD AT KING'S COLLEGE HOSPITAL, LONDON

Diabetes Insipidus with Regressing Miliary Shadows in the Lung.—J. L. LIVINGSTONE, M.D.

E. C., female, aged 46. Married. Nulliparous.

12.9.40: Patient developed a "cold", with temperature (100° for one day) and a cough, during which she noticed a gradually increasing thirst, polyuria, dry tongue, anorexia and lassitude. Symptoms rapidly increased following a land-mine explosion 400 yards away. The cough cleared up in a few days and was replaced by pharyngeal catarrh, which, with the other symptoms, has persisted.

Past history.—Bilateral otitis media in childhood, and chronic right otorrhœa till two years ago. Left ear dry since childhood, but patient suffers from bilateral middle-ear deafness. Tonsillectomy and adenoidectomy at 14 years, and again at 17 years. She had a carbuncle of the right pubis, boil of neck and right "stye" between 8.9.40 and 20.10.40.

Family history.—Nothing abnormal.

On examination.—Apart from a bilateral perforation of the ear drums and catarrhal pharyngitis, there were no physical signs.

Investigations.—Radiographs: Skull, humeri, hands and femora normal. Chest (20.9.40): Diffuse miliary mottling of lung fields. This appearance has persisted, in subsequent radiographs, but there is some regression in pictures taken on 13.3.41.

Cerebrospinal fluid: Normal pressure, clear. No cells. Protein 40 mgm.%. Globulin negative. Pandy and Lange tests normal. Wassermann reaction negative.

Blood: Wassermann reaction negative. Blood cholesterol, 238 mgm.%, taken one hour after light carbohydrate meal.

Blood-count: R.B.C. 5,489,000; Hb. 86%; C.I. 0·97; W.B.C. 6,660. Polys. 57%; lymphos. 32·5%; monos. 8·0%; eosinos. 2·5%.

Blood sedimentation rate (Westergren): 30.10.40, 15 mm.; 2.12.40, 27 mm.; 8.1.41, 15 mm.; 7.2.41, 20 mm.

Progress.—The patient has remained afebrile; diabetes insipidus has been modified by posterior pituitary extract, given by various routes, but polydipsia and polyuria have persisted, although her other symptoms are improved temporarily by treatment.

Recurrent Winter Bronchitis with Fibrotic Stenosis of the Right Lower Lobe Bronchus.—J. L. LIVINGSTONE, M.D.

Male, aged 49, with history of recurrent winter bronchitis since pertussis in childhood. Radiograph in 1932 stated to show opacity at right base. Cough has been persistent with ½ oz. mucopurulent sputum, since September 1940. Cough increased on lying down, and stained sputum produced occasionally during this time. Increasing dyspnœa for six months: has not lost weight recently, but is about 20 lb. below average. Smokes moderately.

Family history.—One sister died of pulmonary tuberculosis in 1907 and another in 1922. One brother stated to have had tuberculosis, but is now in good health. Four sisters alive and well.

On examination.—Weight 9 st. Nervous type. Signs of chronic bronchitis and mild emphysema with asthmatic wheezing: impaired note and air-entry at right base. Blood-pressure, 120/80. Reflexes brisk. Radiograph suggests collapse of right lower lobe, confirmed by bronchogram which shows failure of opaque oil to enter bronchus to right lower lobe; the right chest is filled by upper and middle lobes. Bronchoscopy by R. C.

Brock (27.2.41) demonstrated a stenosis of the right lower lobe bronchus to the size of a match-stick. There were no signs of malignancy: bougies were passed to attempt to dilate the stricture.

The sputum was negative for tubercle bacilli and malignant cells: it contained a mixture of bacteria.

It is suggested that the stenosis may be caused by fibrosis from a neighbouring tuberculous gland.

"Adenoma" of Bronchus treated by Pneumonectomy.—R. C. BROCK, M.S.

Rose C., aged 23. In March 1939 acute febrile illness and thought to have a small left pleural effusion. On examination at Hammersmith Hospital was found to have an atelectatic left lower lobe. In June and in September she coughed up about half an ounce of blood, and on readmission to hospital bronchograms showed gross atelectasis of the collapsed left lower lobe and a filling defect at the origin of the left lower lobe bronchus suggesting a tumour. Bronchoscopy in 1939 confirmed the presence of a nodular mass apparently arising in the bronchial wall and projecting into the lumen from the medial side in such a way as to cause almost complete occlusion of the bronchus. The appearances were of a so-called "adenoma" of the bronchus; biopsy confirmed this diagnosis. Tumours of this type probably arise from mixed bronchial glands situated outside the cartilage of the bronchial wall.

Treatment.—In November the tumour was irradiated by 9 radon seeds each of 2 millicurie strength. At bronchoscopy five months later the tumour was seen to be much smaller but was still visible. In October 1940 she had a sharp attack of pleurisy with sputum, and bronchoscopy showed that the tumour was as big as ever.

In view of the situation of the tumour, the failure of response to radon and the established bronchiectasis of the left lower lobe, it was decided that operation should be advised rather than further radon application. Owing to the position of the obstruction total pneumonectomy was necessary.

Operation.—Total left pneumonectomy was performed by dissection of the hilar structures on February 5, 1941. The patient made an uninterrupted recovery; the chest healed by primary intention and no bronchial fistula developed.

Examination of the specimen showed a nodular tumour arising in the wall of the left lower lobe bronchus and projecting as much outside as inside. It was about 1·5 cm. in each direction. The lower lobe was grossly bronchiectatic, the dilated bronchi being filled with mucopurulent secretion.

Hæmochromatosis Associated with Acanthosis Nigricans.—R. D. LAWRENCE, M.D., F.R.C.P.

S., male, aged 47. Single.

Attended hospital with a history of cramp in the legs, polyuria, thirst, and loss of two stones in weight. These symptoms followed an attack of influenza three months ago. Patient had had an attack of jaundice several years previously.

Past history.—Luetic infection eighteen years ago, treated intensively and said to be cured after two and a half years. There is no relevant family history.

On examination.—He was observed to be pigmented. Spleen and liver enlarged. Blood-pressure, 130/80. The pigmentation of the skin generally brownish, but most marked in the axillæ and groins, and here appeared to be greyish. There was here also early papillomatosis. The generalized discoloration is suggestive of hæmochromatosis, but the axillary appearance resembles changes seen in acanthosis nigricans.

The urine contained sugar and acetone.

Investigations.—Barium meal: normal alimentary tract. Wassermann reaction weak positive. Blood sugar 0·244% at noon. Blood-count: R.B.C. 4,300,000; Hb. 85%. No abnormal forms. W.B.C. 4,400.

Biopsy.—Axillary skin shows slight irregularity of epidermis. Corium: a little perivascular round-celled infiltration. Elastic tissue scanty, but shows no pigmentation. Compatible with acanthosis, but not diagnostic. Skin from leg shows thinning of epidermis with flattening of interpapillary processes. Scattered through the corium and showing well-marked concentration round the sweat glands are large numbers of macrophage cells laden with pigment granules. Most of this gives a positive Prussian blue reaction and tends to mask iron-free pigment which is also present.

Dr. F. PARKES WEBER said he thought that the changes in the axillary skin were insufficient in degree to justify the diagnosis of acanthosis nigricans.

Hirschsprung's Disease: Condition Three Months After Sympathectomy.—R. C. F. CATTERALL, M.Ch., for Lieut.-Colonel HAROLD EDWARDS.

H. S., male, aged 15.

2.10.40: Admitted to hospital complaining of constipation.

Enormous abdominal distension, with splaying of the costal margin. Distension decreased with colonic washouts. Barium enema under spinal anæsthesia produced active incontinence of fæces after about 2 pints of barium had been run in. (Films spoilt.)

26.11.40: Left lumbar sympathectomy. Uneventful convalescence. Incontinent of fæces on the fourth day. Persistent incontinence for a fortnight before control was gained.

18.12.40: Discharged fit.

January 1941: Seen as out-patient. Costal margins regaining normal contour. No ill-effects in left leg following the sympathectomy.

Pulmonary Asbestosis.—PHILIP ELLMAN, M.D.

M. T., aged 45, housewife, worked in an asbestos factory in 1910 for twelve months. She was responsible for sewing asbestos mattresses, which involved the continued association with asbestos dust.

She was perfectly fit until 1933, when she began to complain of breathlessness, persistent cough, and progressive loss of weight and lassitude. She was first seen by me on 19.4.37, when she was obviously breathless. She weighed 10 st. 7¼ lb. Her normal weight was 13 st. She has recently regained the weight she had lost.

The sputum was persistently negative for tubercle bacilli, but Professor Matthew Stewart found asbestos bodies present.

The physical signs in the chest showed impairment at both bases with fine crackling râles heard especially after coughing.

X-ray examination: A characteristic diffuse basal fibrosis, extending somewhat into the middle zones, compatible with pulmonary asbestosis; no evidence of any tuberculous lung infiltration.

The interesting feature in this case is that the patient worked in an asbestos factory for twelve months thirty-one years ago, and she is still coughing up asbestos bodies in her sputum.

Chronic Myeloid Leukæmia.—R. B. NIVEN, B.M., for A. GILPIN, M.D.

Janice W., aged 10½ years.

The patient was a normal, healthy child until the beginning of summer 1940. She then began to lose weight and to suffer from breathlessness and tiredness. She was examined by her general practitioner in July 1940 when, apparently, no abnormality was found. In September 1940 she was seen again and then had splenomegaly. A diagnosis of myeloid leukæmia was made and she was given six deep X-ray treatments at Nottingham. The condition is very rare in childhood.

On examination.—Pale child. Gross splenomegaly.

Blood-count (18.3.41 by Dr. R. D. Clay): R.B.C. 2,250,000 per c.mm. Nucleated red cells = 12,000 per c.mm. Hb. 45%; C.I. 1·00. Total leucocytes 450,000 per c.mm. Myeloblasts 2%, myelocytes 40%, metamyelocytes 13%, polys. 35%, eosinos.* 2%, basos.* 7%, lymphos. > 1%.

* = including E. and B. metamyelocytes.

Pancoast's Tumour.—A. GILPIN, M.D.

Male, aged 49.

History.—Symptoms first began in May 1940, when a dull intermittent ache was noticed beneath the left clavicle. By June 1940 this ache had become more persistent and troublesome. In September 1940 was experienced the first of a series of severer attacks of pain lasting from seconds to many minutes. These attacks of pain were very often occasioned by walking, and he would have to stand immobile for a period to obtain relief. Radiation of the pain into the left side of the neck, into the left arm, and down the inner side of the forearm, and into the back of the chest around the left scapula soon began to be experienced. Hæmoptysis was first noticed in December 1940.

Present condition.—Left-sided Horner's syndrome, weakness in most movements left arm and slight wasting of hypothenar eminence of left hand. There is decreased sensation to pin-prick and cotton-wool in left arm especially marked in ulnar nerve distribution, and relative dullness, flattening, and diminished movement of upper left chest.

Radiograph: Opacity at apex of left lung with erosion of posterior part of third rib.

Familial Multiple Polyposis of the Colon with Carcinomatous Degeneration.
E. EMLYN LEWIS, F.R.C.S., for Lieut.-Colonel HAROLD EDWARDS.

Female, aged 25.

In November 1937, when 22 years of age, patient was seen because of pain in the left side, and a mass could be felt in the region of the splenic flexure. Shortly after this she was operated upon for large bowel obstruction. The mass at the splenic flexure was removed and a transverse colostomy established. On section the mass was shown to be an adenocarcinoma, and the condition of the colon wall suggested polyposis. Sigmoidoscopy subsequently revealed polyps in the rectum.

Early in 1938 total colectomy was performed in two stages. At the first that portion of the colon distal to the colostomy was removed, combined with an ileo-rectal anastomosis. This portion of the colon contained many polyps, one of which had become malignant. Paracolic glands in this area also contained carcinomatous deposits. At a second stage the cæcum, ascending colon, and transverse colon were removed. This specimen also contained polyps, but they were less in number than those in the left side of the colon.

The polyps in the rectum were treated by diathermy on many occasions. In November 1938 the rectum was clear of polyps. She has been inspected every few months since then, and fresh polyps have appeared from time to time. These have been dealt with as they appeared.

It is now nearly three years since her colectomy. At first she passed six to seven motions a day, but now three to four are usual. She has gained considerably in weight.

Family history.—Her father died of carcinoma of the rectum at 44 years of age and within a few months of her operation her brother was found to have an inoperable carcinoma of the rectum from which he died. Her younger sister has been thoroughly investigated and periodically has a barium enema and sigmoidoscopy but no polyps have been seen.

A specimen consisting of part of the resected colon was shown.

Steatorrhœa Associated with Regional Colitis and Chronic Pancreatitis (Specimens and Slides Only).—R. S. BRUCE PEARSON, D.M.

D. E., male, aged 15½ years. First admitted in February 1940, and shown at the Clinical Section in March (*Proceedings*, 33, 414, Clin. Sect., 8). He had had diarrhœa for three to four months before admission, but before this had been unwell for some months, and at one time complained of œdema of the feet. Weight 6 st. 2 lb. at this time; high complexion, prominent abdomen. Stools fatty (83% of dry weight) on a mixed diet and contained blood and pus. On a low-fat diet the stools were watery, but still contained a high percentage of fat (27·6%). He was occasionally pyrexial for a few days, the temperature rising to 99·5°. In spite of a constant low value for his serum protein which was repeatedly found to be below 3 grm. %, he was never observed to develop œdema, and although his serum calcium was never found to be above 7·5 mgm.% he showed no evidence of tetany, and Chvostek's, Trousseau's, and Erb's signs were always negative.

There was partial collapse of the bodies of the seventh and eleventh thoracic vertebræ due to osteochondritis; never any evidence of general decalcification. Hæmoglobin at first 100%. Blood picture normal. Blood sedimentation rate 7.

He remained in hospital with slight improvement for nearly three months on a fat-free diet, and was then discharged. September 1940: readmitted on account of loss of weight and treated by Dr. Hoyle at Horton Hospital. It was then observed that whereas at the time of his previous admission occasional meat fibres only were seen in the stools, these were now numerous. He improved slightly, and was again discharged in January 1941.

February 1941: Seen again as out-patient, extremely wasted, weak, and with some colicky abdominal pain. Readmitted, but gradually went downhill during the next week, and died. Apyrexial during this time.

Post-mortem.—The colon was enormously dilated and thickened and œdematous in its descending and sigmoid portions. Over these regions there were numerous petechial hæmorrhages in the subperitoneal coat and beneath the mucosa. The coils of the sigmoid were matted together to enclose a thick-walled abscess immediately beneath the abdominal wall and above the bladder. The appendix, which appeared to be normal, was included in this. There was some clear fluid in the peritoneal cavity, and a number

of cysts attached to the peritoneum: on microscopical examination these appeared to be dilated lymphatics. Three cysts of the same type as those seen in the abdomen were found adhering to the pleura in the left lung. The pancreas was hard and irregular and divided by numerous fibrous bands. There was no enlargement of the glands at the root of the mesentery. The organs were otherwise normal.

Mercury Poisoning.—G. A. KILOH, M.D.

A. S. E., male, aged 28, married. Thermometer tube blower.

History of previous illness.—Six months ago first noticed trembling of hands. Took up drawing in an attempt to steady hands, but trembling increased and became more or less general. No weakness of legs. Latterly became easily exhausted, felt irritable and depressed, suffered from headaches, and had morning sickness frequently after breakfast, eventually causing him to forgo this meal. Sialorrhœa a definite symptom. No complaint of mouth lesions, or dental trouble.

Past history.—Nothing relevant. Influenza one year ago.

On admission.—He looked ill and restless, obviously rather depressed with expressionless face, definite slurring of speech, slight pallor, slight exophthalmos.

Central nervous system.—Intellectual function normal. Cranial nerves normal. Retinæ normal. Coarse tremor eyelids, tongue, lower jaw, hands, and legs. Arms: No wasting; no fibrillation; accentuated deep reflexes; no sensory changes. Abdominal reflexes normal. Legs: Deep reflexes accentuated; normal apart from tremor.

Cardiovascular system.—Normal. Blood-pressure raised. 180/120, later 152/108. There was no stomatitis.

Investigations.—Blood-count normal. Blood urea 32 mgm. per 100 c.c. Urea clearance normal. Urine contains 1·4 mgm. of mercury (approx.) per litre.

Progress.—Considerable improvement since admission. Now feels well. Tremor only slight. Speech not quite normal.

Spinal Concussion.—S. ORAM, M.R.C.P., for Professor S. NEVIN, M.D., M.R.C.P.

R. K., female, aged 38, single. Shorthand-typist.

On 6.11.40, when standing in a house which was hit by a bomb, the patient was blown backwards about one yard. She did not lose consciousness. For the following three or four days had retention of urine, and also repeatedly vomited during this time. Noticed that slightest stimulation, e.g. person walking past bed, caused extreme pain in both legs.

On examination.—Intellectual function, cranial nerves, arms and trunk normal.

Legs: slight generalized wasting; flaccid, no fibrillary twitchings; no movement of toes or ankles; slight flexion and extension at knees possible.

Reflexes: both knee-jerks brisk, both ankle-jerks absent, both plantar reflexes flexor, and flexor withdrawal reflex present. Stimulation of sole causes extreme agony. Abdominal jerks present all four quadrants, but lower quadrants diminished. Anal reflex brisk both sides.

Sensation: loss bilaterally equal and confined to area below knees. Diminution to pin-prick, cotton-wool, and temperature, greater distally. Area of loss to cotton-wool is less than to pin-prick. Considerable loss of sense of position, and gross diminution of vibration sense at ankles. Muscles of legs and thighs hyperæsthetic to pressure pain. Sphincters normal.

Gait: unable to stand or walk.

Investigations.—Radiograph of spine normal. Lumbar puncture: Pressure 75 mm. Cerebrospinal fluid otherwise normal. Electrical reactions: normal, but slightly reduced.

Progress.—Much return of power to legs: is beginning to walk. Areas of anæsthesia becoming less.

POSTSCRIPT.—1.7.41: Patient now has normal power in both legs and sensation is normal apart from a small area of diminution to cotton-wool near the lateral malleolus of the left ankle. She can walk unaided long distances without trouble.

Dr. F. PARKES WEBER said that, as one knew of destructive lesions in the brain which caused imperception of pain in various parts of the body, it seemed highly probable that minor lesions could also be produced which caused temporary excessive perception of pain. He thought that in some cases like the present one local hyperæsthesia and pain were not rarely attributed to " spinal concussion " when the cause was equally or more likely to be some slight temporary lesion in receptor areas of the brain producing over-sensitivity towards stimuli coming from the periphery.

Athetosis.—S. ORAM, M.R.C.P., for Professor S. NEVIN, M.D., M.R.C.P.

M. S., female, aged 23, single. Toy-maker.

Her mother noticed that at the age of 18 months, the child had tendency to fall over backwards; this became gradually worse, and at the age of four years definite choreo-athetoid movements began. When embarrassed or frightened she finds right arm "wandering away and right leg begins kicking".

Previous history.—Semi-starvation during childhood. Influenza 1928. No history of encephalitis.

History.—One of twins; a breech presentation—no instruments. Other twin died of "convulsions" at 3 months. Her mother had no abortions.

On examination.—Mentality: Co-operates well, but facile. Cranial nerves: slight facial asymmetry due to spasm of right lower face. Spasmodic right internal strabismus. Tremor of eyelids when closed.

Arms: Right, some loss of power. Reflexes present, but difficult to elicit because of mobile spasm. No sensory loss or wasting. Persistent fine tremor present. Left arm normal. Abdominal reflexes markedly diminished in all four quadrants.

Legs: Some wasting present, more marked in right leg. Thigh 9 in. From anterior superior iliac spine: R. 17½ in.; L. 17¾ in. Calf 4 in. From tibial tubercle: R. 11 in., L. 11¾ in. Tendon reflexes exaggerated both limbs, more marked on right. Ankle clonus present both sides. Both plantar reflexes extensor.

Sensation normal. Sphincters normal. Choreo-athetoid movements involve mainly right side of body, but left arm and face also affected. Walks in typical spastic manner. Movements cease during sleep.

[*April* 24, 1941]

MEETING HELD AT THE BRITISH POSTGRADUATE MEDICAL SCHOOL, LONDON

TWO CASES SHOWN BY J. MCMICHAEL, M.D.

I.—Spinal Neurofibroma. ? Disseminated Sclerosis.

Male, aged 45.

19.3.41: Admitted to hospital complaining of pain and weakness in right arm, pains between the shoulder blades and weakness of the right leg.

History.—Ten years ago, after an acute illness with vomiting, noticed right leg weak. About the same time a painless lump began to appear on the back of the right forearm. Received a course of injection treatment at weekly intervals. Leg became stronger and he returned to work. Weakness of right leg became so marked that he could not continue work. In past seven years strength of leg has varied. Few years ago lump in forearm became painful if knocked, and recently there has been spontaneous pain. For one year the right hand has been weak. For one month there has been an aching pain between the shoulders.

Family history.—Nothing relevant.

On examination.—Nystagmus. Pallor of temporal half of right disc. Wasting of small muscles of right hand. Wasting of right triceps. Deltoids—fair power in both. Unsteadiness with right hand. Abdominal reflexes absent. Plantar responses extensor. Right leg weaker than left. Impaired vibration sense in right foot. Impaired joint sense both great toes.

Lumbar puncture: Pressure 70 mm.Hg. Queckenstedt's test normal. Wassermann reaction normal.

Biopsy of forearm tumour: Perineural fibroma.

POSTSCRIPT.—July 1941: Lipiodol injection showed no spinal block. Final diagnosis: Disseminated sclerosis.

II.—Gaucher's Disease.

Male, aged 30.

21.3.41: Admitted to hospital.

History.—Right leg amputated for "osteomyelitis", aged 16.

1936: In this hospital with splenomegaly. Areas of increased translucency of bones. Leucocytes ranged from 7,000-50,000 with normal differential count.

1941: Complained of general malaise, pain in the back and some thirst.

Family history.—No history of the disease, but paternal grandfather's family cannot be traced.

On examination.—Pigmentation over pressure areas and over left ankle. Fan-shaped brownish-yellow pingueculæ lateral to corneæ. Spleen enlarged to umbilicus. Liver not felt.

Special examinations.—Lipoid nitrogen 29 mgm.% (normal 15-25). Gaucher cells found in sternal puncture. X-rays show typical bone changes.

Rheumatoid Arthritis with Rheumatic Heart Disease.—E. G. L. Bywaters, M.R.C.P.

Female, aged 31.

Admitted complaining of swelling and pain in the joints.

History.—Attacks of rheumatic fever when aged 6, and again when aged 18. Between and after these the patient has led a normal and symptomless life, having a normal pregnancy at the age of 26.

Sixteen months ago, onset of swelling and pain in right 3rd proximal phalangeal joint. The metacarpophalangeal joints became swollen and stiff and then (eight months ago) the knees and ankles. There have been fluctuations and variation in the joints affected, but at one time or another most joints have been affected.

She has had no skin rashes or nodules, no dyspnœa or swelling of the feet. No sore throats.

On examination.—The heart shows mitral stenosis and aortic regurgitation. Blood-pressure 120/80.

The hands are weak and there is swelling of five metacarpophalangeal joints and of the right 3rd proximal phalangeal joint. The right wrist is swollen and limited, and there is wasting of both arms.

The left knee contains fluid and shows thickened membrane: the left ankle is swollen and painful, as are the left mid-tarsal joints. There is wasting of the left leg.

Electrocardiogram shows bifid P_2.

Radiographs: Hands: General decalcification of carpus and wrist-joints, subchondral rarefaction of three finger-joints and diminished joint space in right wrist and two finger-joints.

Heart: Slight enlargement of left ventricle and prominence of conus arteriosus.

Blood-count: Hb. 80% ; W.B.C. 14,000 with 80% polymorphs.

Sedimentation rate: 103, 90, 85, 80, 90, 65 mm./hr. (Westergren).

Aspiration of knee-joint: 28 c.c. cloudy yellow fluid at a pressure of 150 mm. H_2O, not clotting, containing 5,800 leucocytes (polys. 80%, leucos. 10%, monos. 10%). The sugar was low (75 mgm.% compared with 93 mgm.% in the blood), and the protein comparatively high (5·9 g.% compared with 7·8 g.% in the blood). Bacteriological examination negative. This fluid resembles that of rheumatoid arthritis rather than that found in rheumatic fever.

Rachitic Flat Pelvis—Delivery by Natural Passages.—Meave Kenny, M.R.C.O.G.

(5347/40.) L. G., aged 34. A short slight woman, a native of Hungary—height 5′ 1″. Expected date of delivery 9.9.40. First pregnancy. Hypertension developed at 24th week but settled to normal with rest. At the 36th week œdema and hypertension recurred but again subsided with rest in hospital. The fœtal head was lying in the R.O.L. well above the brim and would not push in. Lateral and stereoscopic antero-posterior views of the pelvis showed a classical rachitic flat configuration. The brim was flattened, C.V. 3·1 inches, with acute forward angulation of the lumbosacral articulation, and minimal side-to-side concavity of the sacrum. The sciatic notch, however, was characteristically wide and shallow, the ischial spines insignificant. The fore pelvis was somewhat android.

The patient came into hospital in labour on 6.9.40. The head was still free. Uterine contractions were scarce and poor at first ; omnopon-scopolamine analgesia and the administration of a single large dose of œstrogen followed by ½-hourly pituitrin (2 units) improved the pains and brought the head through the brim in the R.O.T. into the mid-pelvis. Vitamin K was administered to the mother throughout the four days of labour. Manual rotation of the head into the O.A. was carried out and a 7 lb. 11 oz. child delivered by forceps with great ease. There was very marked overlap of the parietal bones, the child was of good colour, cried at once, and is still thriving. The total duration of labour was 102 hours, but at no time was the patient distressed, and her condition in the puerperium was satisfactory.

Intraperitoneal Bleeding from a Ruptured Uterine Vein in Pregnancy.—K. M. D. HARDING, M.R.C.O.G., F.R.C.S.E.

Mrs. P., aged 33. Primigravida. 26 weeks pregnant.

15.3.41: Admitted almost moribund as "concealed antepartum hæmorrhage", with a history of severe abdominal pain following coitus about twelve hours prior to admission.

On examination.—Patient collapsed, shocked. Temperature 96. Pulse 120. Respiration 26. Blood-pressure 62/48. Uterus the size of 26 weeks' pregnancy, very tender. No albumin in urine.

Treatment.—Morphia, blood transfusion, subsequent laparotomy.

Blood, 3 pints or more, was found free in the peritoneal cavity, the origin of which was only located after an intensive search, and was found to be from an area on the posterior wall of the uterus.

The oozing area was under-pinned with sutures, a hysterotomy performed and a still-born 24 weeks' fœtus removed.

Large veins were seen radiating from the placental site and it was possible to conjecture one of these, now collapsed, leading to the traumatized area.

The area of lesion on the posterior wall of the uterus would in position have coincided with the sacral promontory; it is suggested therefore that during the act of coitus the vein was ruptured against the promontory.

Carcinoma of the Thoracic Œsophagus treated by Œsophagectomy.—R. H. FRANKLIN, F.R.C.S.

Mrs. A. D., aged 51, was seen on 6.3.41 presenting the following history: One year ago she had an attack of nausea and vomiting, bringing up material which seems to have resembled "coffee ground" vomit. Treated at home by her own doctor for a few days, then returned to work. She kept at this for nine months, feeling well and not losing weight.

Three months ago she started to get dysphagia with solid food accompanied by pain in the region of the xiphisternum and regurgitation. She noticed that the regurgitated food contained small quantities of blood at times. The dysphagia progressively increased until she was able to take liquids only. During three months she lost nearly a stone in weight. On admission she weighed 6 st. 2 lb. 8 oz. Apart from emaciation, physical examination failed to show any obvious abnormality. Her blood-pressure was 180/105.

Investigation.—8.3.41: Blood-count: R.B.C. 4,600,000; Hb. (Haldane) 90%; C.I. 0·96.

10.3.41: No occult blood in fæces.

11.3.41: X-ray examination (Dr. Duncan White) showed an obstructive lesion at the level of the 8th dorsal vertebra and extending for 2½ in.

13.3.41: *1st operation.* Stomach and available portion of liver examined, no abnormality found. Kader-Senn gastrostomy performed.

8.4.41: *2nd operation. Œsophagectomy.* The œsophagus was approached from the left side of the neck and the right side of the thorax. The pleural cavity was drained by means of a de Pezzer catheter which was connected to a water-seal bottle. The œsophagus was left lying across the chest until evening when it was excised just above the growth and a tube tied into the stump of the œsophagus.

10.4.41: Chest drain removed. Patient very well.

17.4.41: X-ray examination of chest showed almost complete re-expansion of right lung. Tube from œsophagus connected with gastrostomy.

The patient can drink freely through her rubber "œsophagus" but still prefers to have her gastrostomy feeds as before on account of the taste of the halibut liver oil.

POSTSCRIPT.—5.7.41: Patient is taking all meals by mouth and is gaining weight at the rate of 1 - 2 lb. per week.

Hind-quarter Amputation for Chondrosarcoma.—DOROTHY SPENCE-SALES, M.B., for Professor GREY TURNER.

G. T., aged 49. Male.

History.—Admitted in June 1940 complaining of aching pain in the left buttock and a swelling in the left groin of three months' duration. On examination a smooth hard tumour was felt 2 in. above Poupart's ligament and extending from the anterior superior spine of the ilium to the symphysis pubis. X-ray showed the presence of a generalized osteitis deformans and in the left ilium local bone necrosis and palisading new bone

formation which was diagnosed as malignant change. On 18.6.40 local excision of the tumour was performed (Incision: parallel to and above Poupart's ligament from symphysis pubis to halfway along iliac crest). Pathological examination of the excised tumour showed that it was a chondrosarcoma. The patient was discharged a month later and put on a course of Coley's fluid m½ weekly.

In November 1940 X-ray showed further destruction of bone and by January 1941 the tumour had extended to the outer aspect of the left ilium overlapping into the inter-trochanteric region. There was, however, no evidence of secondaries in the lungs and in view of the facts that pain was increasing and deep X-ray therapy had had no effect on the growth it was decided to carry out a hind-quarter amputation.

Operation (30.1.41).—Surgeon: Professor Grey Turner. Anæsthetist: Dr. Woodfield Davies.

Anæsthetic: (1) Pre-operation: Omnopon gr. ⅓, scopolamine gr. 1/150. (2) Spinal: 2 c.c. 1% novocain. (3) Gas, oxygen and ether. (4) Local injection sciatic nerve and lumbar plexus. Intravenous 5% glucose saline and blood given by drip transfusion from beginning of operation.

Incision.—This was made just below the previous scar and extended backwards along the iliac crest and downwards towards the symphysis pubis. The peritoneum adherent to the scar was opened and the growth found to extend from within 2 in. of the pubic ramus to just short of the sacro-iliac joint, the soft tissues and muscles being stretched over it. The peritoneum was closed and stripped off the lateral pelvic wall as far as the common iliac artery on which a temporary ligature was placed. The incision was then carried down to the inner aspect of the thigh round the back of the thigh to join the main incision. The muscles attached to the iliac crest were completely divided, the soft parts overlying the tumour reflected inwards and the external iliac vessels ligated and divided. The levator ani was cut along its whole attachment but the internal iliac vessels preserved for maintaining the nutrition of the flap. After injection of the great sciatic nerve and the lumbosacral cord the iliopsoas was divided, thus completely separating the limb. Redundant skin flap was excised, interrupted catgut sutures used to approximate muscle tissue over the peritoneum and the skin edges brought together with interrupted silkworm gut sutures. A drainage tube was left in and brought out through the upper end of the wound.

Time of operation.—Two hours.

Comments.—Considering the extent of the operation there was no undue loss of blood. One hour after operation the systolic B.P. dropped to 55, the pulse was almost imperceptible and the patient was sweating profusely. By twenty hours later a total of 1,500 c.c. of blood and 1,000 c.c. of 5% glucose saline had been administered and the B.P. was 105/70, and the pulse volume much improved. An intravenous drip of 1,000 c.c. of plasma was then begun.

Progress.—General condition improved. 9.2.41: Purulent discharge (*B. coli*) from the wound. 18.2.41: Blood-count showed R.B.C. 2,100,000. Transfusion 540 c.c. blood given. 19.2.41: Large slough in wound removed with scissors. 20.2.41: Started on a course of ascorbic acid 1,000 mgm. daily for five days.

From then on the patient has continued to improve, and although there has been pocketing of pus and discharge from the wound, slow healing continues.

Postscript.—June 1941: Patient wrote to say he felt well and was making steady progress.

Renal Aneurysm.—D. M. Douglas, F.R.C.S.

A. T., male, aged 59. Married. Engineer.

Admitted 15.10.40 with complaint of two attacks of right-sided abdominal pain with hæmaturia, the first attack three weeks before the second on the day of admission.

Previous history.—1905. Westminster Hospital. Exploration of the left kidney for abdominal pain. No abnormality found after incision into lower pole and digital examination of pelvis.

Physical examination was essentially negative.

Investigations.—Normal blood-count. Blood urea 40 mgm. per 100 c.c. Urine: Large number of red cells. Few leucocytes. Small growth of *Staph. albus.* X-ray: Large circular opacity in left kidney.

Pyelograms: Intravenous. Poor definition on the right, slight hydronephrosis on left, with large opacity in inferior major calix.

Retrograde: Normal right pyelogram.

Chromoscopy: Right: Good concentration in ten minutes. Left: Fair concentration in eleven minutes.

Provisional diagnosis.—Large left renal calculus with the corollary that the peculiar peripheral density of the shadow suggested the possibility of calcification in an old hæmatoma or cyst.

Operation (13.11.40).—Left nephrectomy. Lumbar approach. Dense adhesions around the lower pole. The calcified mass in the lower calyx was found to indent between the fingers and to give characteristic egg-shell crackling and when a knife was inserted, arterial blood gushed out, pulsating simultaneously with the heart beat.

Nephrectomy: The specimen proved to be an aneurysm of the lowest branch of the renal artery.

Convalescence uneventful.

THREE CASES SHOWN BY E. P. SHARPEY-SCHAFER, M.R.C.P.

I.—Myxœdema and Dwarfism.

A. C., female, aged 48.

History.—In infancy teethed, walked and talked at the normal age. No growth after the age of 10. Always of low mental standard. Menarche aged 21, regular up to six months ago; since then amenorrhœa. For ten years has felt the cold, has increased in weight, and noticed changes in hair and skin. Three years ago given thyroid for a month; otherwise no treatment.

On examination.—A disproportionate dwarf with protuberant abdomen. Slight mammary development. Skin dry. Hair dry and defective. Voice hoarse. Face puffy. Bradycardia. Some enlargement of heart.

Basal metabolic rate −32%. Blood cholesterol 180 mgm./100 c.c.

Electrocardiogram: Low voltage curve.

X-rays: Heart enlarged. Bones: All carpal bones fully ossified. Epiphyses normal and united. Sella turcica normal. Bones of the vault relatively dense.

No response to injected pituitary thyrotrophic hormone.

It is suggested that the dwarfism is not related to thyroid deficiency.

II.—Cretinism.

F. F., male, aged 8.

History.—Diagnosed as a cretin, aged 9 months, and treated with thyroid ever since.

22.11.40: Thyroid stopped. Since then has become more lethargic. Skin has become thickened and dry.

25.3.41: Basal metabolic rate −46%. Blood cholesterol 420 mgm./100 c.c.

No response to injected thyrotrophic hormone.

Bone age normal.

After five months without thyroid the electrocardiogram has not changed.

III.—Myxœdema.

A. W., female, aged 68.

7.4.39: Admitted with right-sided hemiplegia and hypertensive heart disease.

18.10.39: Diagnosed as myxœdema. Given thyroid, 4 gr. daily till 5.12.39. Showed signs of left heart failure. Thyroid stopped and none given since. Now shows classical signs of myxœdema with large pouches below the eyes, most marked on right side.

Blood cholesterol: 5.12.39: 107 mgm./100 c.c. 16.1.41: 280 mgm./100 c.c.

Serial electrocardiograms show progressive fall in voltage, complicated at one stage by changes probably due to left ventricular failure.

No response to injection of pituitary thyrotrophic hormone.

Section of Urology

President—T. E. HAMMOND, F.R.C.S.

[*March* 27, 1941]

DISCUSSION ON PERSONAL EXPERIENCE OF INJURIES TO THE GENITO-URINARY TRACT

Mr. G. E. Neligan: I propose to take each section of the genito-urinary tract and deal with each in three categories, those injuries I had to deal with in a casualty clearing station in the last war, those experienced during air raids in the present war and those met with in peacetime.

Renal injuries.—When I consider the very large number of abdominal wounds I have operated on the number of cases of renal injuries have been comparatively small. This is easily explained when one considers the important structures in the neighbourhood of the kidney, and that it was not often that the kidney alone was injured. A bullet, shrapnel ball or piece of high-explosive shell passing through the kidney may easily do severe damage to the liver, spleen or large abdominal vessels; or they may travel upwards and injure the lungs. Most of these cases must have died almost at once, or on their way back to the C.C.S., from hæmorrhage and shock; and a good many arrived quite unfit for operation and did not recover despite attempts at resuscitation.

I cannot tell you the number I operated on during my two and a half years with a C.C.S. as all the records were sent into the pool, but they were not a great many. I performed only a dozen nephrectomies in that time.

One saw the through-and-through bullet wound in the loin, which from its direction was only likely to hit the kidney and the signs were of mild hæmaturia and no evidence of other intra-abdominal injury. They usually got well if left alone. Again there was the shell fragment which lodged in the kidney. Here was a lacerated wound requiring excision, and after removal of the piece of shell as one felt the kidney might recover, the wound was just drained. On the other hand, the through-and-through wound that from its direction or abdominal signs suggested injury to the colon or other neighbouring organs, required complete excision and exploration, which could be done through a kidney incision going forward into the abdominal cavity. Whether the kidney was left or a nephrectomy performed depended naturally on its condition.

When the exit was elsewhere in the abdomen or there was no exit, but signs of intra-abdominal injury, the wound in the back or loin was excised first and then a laparotomy performed. It is important that all back wounds should be dealt with before the laparotomy, as if this is done first and the patient then turned over there is a great deal of extra shock. Most cases needed a nephrectomy. About 50% of all abdominal wounds operated on died, so the renal recoveries would be few.

I never saw a renal injury in which one could do a plastic operation; in any case it would have been too risky.

So far I have only had experience of two air-raid renal cases at the London Hospital.

One was a girl admitted with a badly fractured pelvis owing to having been buried under débris. She was very severely shocked on admission and it was many days before she looked like living. On admission a catheter was passed and a little clear urine followed by bright red blood was withdrawn. She was too ill for any investigations so I fixed in a Malecot catheter *per urethram* to put her bladder at rest. The hæmaturia lasted for about ten days. From the severity of the pelvic injury I put it down to an injured bladder. She had no pain in the back or loins.

After a fortnight her temperature began to rise and she gradually developed a large lump in her right loin extending down to the level of the anterior superior spine and almost across to the umbilicus. Although she had never complained of any pain in her chest, X-rays revealed a fracture of the 12th rib. Thinking it was a perinephric abscess I fomented it and after several days she passed a large amount of pus in her urine and the swelling gradually disappeared. An intravenous pyelogram then showed the kidney to be normal and secretion perfect. She left hospital well except for a trace of pus in her urine, and culture still grew *B. coli communis*.

The other case was a man admitted with concussion and a minor head injury. He had hæmaturia and slight tenderness and pain in his right loin. It cleared up in five days and an intravenous pyelogram was normal, showing it was simply a contusion.

Of cases occurring in peacetime I have collected the records of the last twenty years at the London Hospital and those I have seen privately. I have dealt with 11 cases, seven of which were simple contusions, and the other four required operation. The former are by far the commonest renal injuries and result from minor injury to the loin, and usually the only sign is hæmaturia which clears up in a few days with rest. Four were due to football injuries, two to falls on the side and one to fracture of three lumbar transverse processes. All except one cleared up in a few days, the exception lasting for nearly three weeks, but this ceased and an intravenous pyelogram was normal.

Of the four serious cases one was a severe injury to the loin and the other three hæmorrhage into pre-existing hydronephroses following injury.

The first developed an increasing hæmatoma in the loin and severe hæmaturia. There were no signs of intra-abdominal injury. I operated through a loin incision and found the lower pole of the kidney almost completely detached, the rest of the kidney not being seriously injured. I removed the lower pole and sutured the kidney and the patient recovered.

Of the hydronephroses, the first case was a boy kicked in the left loin while playing football. He had hæmaturia, which subsided in a few days, but every time he got up the hæmaturia recurred. I did a pyelogram and found a fairly large hydronephrosis due to an aberrant artery, so performed a nephrectomy. He had had no previous renal symptoms.

The second was also due to a kick in the left loin received while playing football and he had severe hæmaturia and pain. It subsided and he was sent into hospital under my care as he had a large swelling in the left loin. The only previous history was of occasional mild attacks of pain in the left iliac fossa. A retrograde pyelogram showed a large hydronephrosis, which I removed.

The third was a big game hunter who had wounded an elephant, which then charged him. In attempting to step behind a tree he fell and the elephant straddled him and hit him in the abdomen with the base of his trunk. He was carried to a mission hospital and had hæmaturia for several days. He returned to England and I was asked to see him as he had repeated attacks of painless hæmaturia. There was no history of previous renal symptoms, but a retrograde pyelogram showed a very large hydronephrosis due to an aberrant artery. I did a nephrectomy.

These cases indicate that hæmaturia following an accident which does not clear up quickly or which recurs should have a complete renal investigation.

I have had no cases of run-over accidents requiring laparotomy and abdominal nephrectomy, though as a house surgeon I remember assisting with two.

During the last twenty years 58 cases of renal injury have been admitted to the London Hospital, of which 42 were simple contusions and 16 were serious injuries, 2 in hydronephrotic and the other 14 in otherwise normal kidneys. Two died shortly after admission, and the others had abdominal nephrectomies, of whom four died.

These numbers are surprisingly small, but the person who is run over by the modern car or bus and ruptures his kidneys is almost certainly killed at once and so is not admitted to hospital.

Ureter.—I never saw a case of ruptured ureter in the last war, though I may have missed them; but in searching through the abdominal contents of a war abdomen, which is probably full of blood, fæces or rations, there is not much chance of seeing an injured ureter. Nor have I seen any in peacetime, except those due to surgical injury.

Bladder.—The chief difficulty with war wounds of the bladder was that they were usually complicated by injury to the sacrum or pelvic bones; very often they were caused by shell fragments entering the buttock. Except where there was an exit it was difficult to know where a buttock wound led to. Most bladder wounds were intraperitoneal as the excitement of warfare did not encourage a full bladder. Where possible an X-ray might

show you the track of the missile if still retained, and a catheter whether the bladder was injured. It was always necessary to excise wounds and remove bone splinters, and if leading to the bladder to drain them. The patient was then turned over and a laparotomy performed. The fragment of shell might be found in the bladder, which should then be sutured and drained suprapubically. If intraperitoneal, the damaged intestine had to be dealt with first and the bladder wounds sutured and drained extraperitoneally. If the rectum was perforated it was best to do a temporary colostomy, as there was no chance of healing as long as the wound was contaminated by fæces.

I have seen only one bladder wound in the recent air raids. The missile entered the patient's buttock and ruptured not only his bladder but several coils of intestine, and he died.

In peacetime rupture of the bladder is usually associated with fracture of the pelvis. I have had only one case, an extraperitoneal rupture. He had pain in the right loin and hæmaturia. I diagnosed a ruptured kidney, but cystoscopy showed a tear in the anterior wall of his bladder. I did a suprapubic cystotomy and repaired the rent round a de Pezzer catheter. He subsequently died of sepsis.

I think that when a rupture is suspected of being extraperitoneal from the fact that the patient passes urine or a quantity is drawn off on catheterization, then a cystoscopy can do no harm and shows where the rupture is.

In the last twenty years at my hospital there have been ten cases of ruptured bladder, seven due to fracture of the pelvis, of whom two died, and three during operations for femoral herniæ.

Urethra.—War injuries of the urethra were uncommon and were usually associated with lacerated wounds of the genitalia or of the pelvis; some were simple through-and-through wounds that just needed repair, while I have known the whole penis shot away. In such a case it was necessary to excise the wounds and tie in a catheter. In wounds involving the pelvis the wounds had to be excised, the splinters of bone removed and a suprapubic drainage was usually necessary owing to the wide laceration of the urethra and surrounding structures.

So far in air raids I have seen one case of ruptured urethra, which was due to a fractured pelvis, the whole front of the pelvis being displaced downwards. Cystotomy had been performed but no effort made to repair the urethra owing probably to the patient being too shocked to stand it. He was transferred to the London Hospital under me a week later and developed bronchopneumonia the next day, so that he was not fit for operation for another four weeks. A metal bougie was then passed suprapubically into the proximal end of the urethra, an external urethrotomy was performed and the stricture incised and a catheter fixed in for ten days. There was a good deal of distortion of the urethra owing to the fractured pelvis. He is now healed and has left hospital, passing urine naturally, and is attending for periodic dilatation.

In peacetime I have had 14 cases of ruptured urethra to deal with, 11 of the penile urethra and the other 3 ruptured between the membranous and prostatic urethras. Of the 11 cases 4 were partial ruptures of the bulbous urethra, due to falling astride a blunt object. One was slight and recovered with no treatment, and the others cleared up after a catheter had been tied in for ten days. Of the 7 complete ruptures at the bulb, on 2 external urethrotomies were performed and the urethral ends sutured round a catheter. In the others a retrograde bougie was passed through a suprapubic opening to make identification of the proximal portion easier, followed by an external urethrotomy, and suture of the urethra round a catheter. After ten days the catheter was withdrawn and periodic dilatation carried out.

Some of you will remember Sir William Wheeler's paper on ruptured urethra read before this Section in January 1929 (*Proc.*, **22**, 469, Sect. Urol., 31). In the subsequent discussion everyone agreed that the correct treatment was to do a suprapubic cystotomy, pass a retrograde bougie, and then do the external urethrotomy and repair. I prefer an indwelling urethral catheter, as I have known cases in which this was not employed and a subsequent internal urethrotomy was required.

The three cases of rupture between the membranous and prostatic urethra all showed dislocation of the prostatic urethra and were due to fractured pelvis. One case was of more than a year's standing when I saw him and he had a suprapubic cystotomy. I passed a bougie through the penile urethra and cut down on it when it impinged on the bladder wall, and then tied in a large Coude catheter. Owing to fibrosis it was impos-

sible to get the two ends of the urethra into alignment. He attended the stricture department for a year and then went to Canada. Dilatation was quite easy.

The other two were fresh cases. They had distended bladders and a catheter stuck past the membranous urethra and only drew off a little blood-stained urine. I performed a suprapubic cystotomy, placed my finger in the dislocated prostatic urethra and manipulated it opposite the membranous urethra. A catheter passed down the anterior urethra could then be guided through into the bladder, acting as a splint and restoring the alignment. After ten days the catheter was removed and the resulting stricture dilated.

In the last twenty years there have been 33 cases of ruptured urethra at the London Hospital, of which 15 were partial and 18 complete.

At the first meeting of the International Urological Society just after the last war this was one of the subjects discussed and the late Frank Kidd was the British rapporteur. I collected for him 44 cases that had occurred at the London Hospital during the previous ten years, and this figure shows a large falling off in numbers during the last twenty years, owing to the establishment of the L.C.C. Hospitals.

Genitalia.—In the war I saw cases of injury to the penis that varied from simple bullet wounds not requiring operation to complete avulsion of the penis. I managed to restore one case of severe laceration of the penis to a normal-looking organ, but what the after-effects of the multiple scars were, I dread to think.

In peacetime most injuries are simple hæmatomata requiring no treatment. The only severe injury I have seen was in a small boy who suffered from nocturnal enuresis. Dreading his parents' displeasure he tied a piece of string tightly round his penis, with the result that the end sloughed off.

War injuries of the scrotum and testicles were either slight or severe lacerations requiring excision and suture; attempts were always made to save the testicles unless they were completely destroyed, when orchidectomy was necessary.

In peacetime the only injuries usually seen are cases of hæmatocele or hæmatomata of the scrotum.

Mr. Jocelyn Swan said he would mention just one case of particular interest. An officer had a machine-gun bullet enter in the left scapular region and come to rest behind the right hip-joint. In its course it perforated the pelvis of the right kidney and slightly lacerated its lower pole. During the following week there was an increasing swelling in the right loin with a rapidly increasing leucocytosis to 23,000 and a polymorph percentage of over 90. Thinking that the perinephric infection had occurred he opened the loin and was astonished to find that the swelling consisted of a large collection of perfectly clear urine from the opening in the renal pelvis. He asked if it was usual for a collection of apparently uninfected urine in the tissues to produce a high leucocyte count in the blood?

Injuries to the ureter were distinctly uncommon, but he had seen more than one case in which a ureter was damaged in the course of an operation for abdominal hysterectomy and two cases in which the left ureter was divided during an abdomino-perineal resection of the rectum. In both of the latter the kidney had to be sacrificed as there was no possibility of a plastic repair of the ureter nor of its implantation into the bladder.

He had seen the bladder wall lacerated during the operation of litholapaxy at the hands of an expert and he had himself had the unfortunate experience of perforating the bladder wall by a cystoscope during the examination of a tuberculous cystitis. Gunshot injuries of the bladder were as a rule very serious lesions as they were so frequently complicated with wounds of the rectum or with extensive compound fractures of the pelvis. He had seen two cases in which fragments of shell were present in the bladder without perivesical extravasation of urine. One patient had had extensive gunshot fracture of the pubis with laceration of the bladder which was followed by a urinary fistula in which numerous calculi were formed, requiring frequent operations for their removal.

It was not perhaps sufficiently realized that the base of the bladder might be seriously damaged during the treatment of a carcinoma of the cervix uteri with radium. He had seen very acute œdema of the trigonal area after radium treatment of the cervix; in one case there was complete anuria for four days. In other cases at a later stage, with the growth under control, there had been the formation of a large vesico-vaginal fistula, rendering the patient's life miserable from constant soakage with urine. In two of these cases he had obtained very considerable relief by transplantation of ureters into the pelvic colon.

(For more complete account *v. Brit. J. Urol.*, 1940, 12, 161 and 221.)

Mr. John Everidge: In *gunshot wounds of the kidney* it is notorious in what a large proportion the entry or exit wound is far from the loin, and how frequently missiles entering the loin miss the kidney, but damage other viscera. Wounds or ruptures of the kidney often give the signs and symptoms of the acute abdomen. In doubtful cases the abdomen must be explored and I prefer to explore the abdomen first, by anterior or transverse laparotomy. The kidney is dealt with *secundum artem* after the peritoneum is closed. A kidney so severely damaged as to require revision lies in a hæmatoma which will have conveniently mobilized the peritoneum and so rendered renal exposure all the easier. When considering conservative surgery of the kidney the possible consequences must be remembered: secondary hæmorrhage, hydronephrosis, persistent sepsis, calculi and, as in a case I have had recently, a late developed fistula.

Ruptured bladders seem more common from accidents among the Forces than from battle casualties. Fractured pelves are too common in these days of mechanized warfare. Thus in the whole series extraperitoneal rupture is far commoner than intraperitoneal.

In extraperitoneal, where there is generally a grave associated orthopædic problem, great assistance will be rendered to the orthopædist if anterior water-tight drainage is established. In intraperitoneal ruptures, however caused, every effort must be made to suture the gap efficiently, but I do not think it safe to omit anterior extraperitoneal drainage. It will not increase sepsis or delay convalescence.

Crush injuries with renal impairment constitute a new syndrome of which I have no knowledge previous to recent air-raid activity. Air-raid and not battle casualties appear singled out and in each of the recorded cases prolonged crushing appears to be the dominating influence. The mortality is very high, death from uræmia on the seventh or eighth day being singularly constant.

I have had two cases, one a girl of 11 who lay crushed for three hours under a heavy beam. Hæmaturia and anuria aroused the suspicion of ruptured bladder, but the absence of pelvic fracture and conclusive physical signs negatived this. Great œdema of the left thigh, evidently injured by the beam, developed, but unaltered peripheral pulse indicated that the swelling was not a hæmatoma. Subsequently œdema became universal and the blood urea rose to 369 mgm. per 100 c.c. before death. All efforts to procure diuresis failed. Autopsy revealed absence of signs of gross trauma in the left thigh or elsewhere. The kidneys were large and pale; microscopically the collecting tubules revealed degenerate epithelium and their lumina packed with, apparently, the debris of red corpuscles. Two negative points are noteworthy in the case, the absence of muscle trauma and that blood transfusion was not given, for both have been blamed as causative. My second case was a male, aged 32, who came under my care convalescent, but the blood urea was still raised to 68 mgm. per 100 c.c., and there was œdema of both ankles, and, oddly enough, much marked in the left thigh; the urine contained blood and albumin but the output was normal. He was evacuated to a safe area as soon as possible. I have recently learned that he has now recovered completely and that the blood urea is 30 mgm. per 100 c.c.

Mr. Zachary Cope remarked that it should not be taken as a matter of course that the treatment of a persistent urinary fistula should be nephrectomy; a transplantation of the ureter into the large bowel ought to be considered and practised if possible.

One of the most difficult injuries of the urinary tract with which he had ever had to deal was a case of rupture of the urethra (due to fractured pelvis) in which the portion of the urethra next to the bladder had been torn off and at operation was found hanging free in a bruised and flabby condition and attached to the neck of the retracted and distended bladder. A gap of more than an inch was found between the two injured parts. The bladder was opened suprapubically and with difficulty a catheter was passed up the urethra into it. When healing took place a long tortuous stricture remained. This necessitated the frequent passing of bougies for which an anæsthetic was usually required. After some years stones formed in the bladder and suprapubic cystotomy was needed. In the end infection of the kidneys led to a fatal issue.

Looking back on this case Mr. Cope thought that it would have been wiser to transplant the ureters into the rectum before renal infection had occurred.

Mr. Geoffrey Parker commented on the effect of blast on the urinary apparatus. At post-mortems done on a series of such cases, not associated with other injuries, one of the most striking features had been multiple hæmorrhages into areas of loose areolar tissue about the body. In the majority of these cases, extravasation of blood, usually in small

quantities, had been noted in the perinephric spaces, and under the peritoneum covering the bladder in particular.

In this connexion he had seen a case of a girl of 17, with blood in the urine. She had no apparent injury, but complained of pains in the back, and exhibited profound shock, which failed to react to the usual stimuli by means of blood and plasma transfusion, electric cradle, &c.

Catheterization gave a specimen of blood-stained urine which might reasonably have been suspected of being due to a lesion of the urinary tract alone, and one requiring surgical intervention after further investigation.

Cystoscopy showed that the bleeding, which was small in amount, was coming from many small ruptured vessels in the bladder wall, and the sluggish efflux from the ureteric orifices was clear. The girl died forty-eight hours later, and at post-mortem was found to have all the classic lesions now associated with a pure blast effect. These included hæmorrhages under the vesical peritoneum, and no gross lesion of the urinary tract.

This experience indicates that if the physical signs, which must include failure to react to anti-shock and anti-hæmorrhage treatment, combined with a suggestive history of the bombing incident, make a diagnosis of blast likely, then the presence of blood in the urine is not necessarily an indication of a surgical lesion of the urinary tract. This would appear to confirm the wisdom of Mr. Neligan's attitude of expectant caution when considering these cases of hæmaturia without collateral signs of injury to the urinary apparatus.

Mr. E. W. Riches considered that one of the greatest changes, as between the last war and this, had been made by the advent of excretion urography in dealing with renal injuries.

He cited two cases of crush injuries to the kidney, in one of which the excretion pyelogram had demonstrated the extent of the injury and in the other where it had shown that the opposite kidney was functionless. In both cases expectant treatment had proved successful.

Mr. John Scholefield said that at the large County Council hospital at which he worked it had been their experience also that injuries of the kidney necessitating operative procedures were uncommon. Cases presenting slight to moderate hæmaturia were not infrequent but only three had led to operation and nephrectomy in the past eighteen months. Of these two were found to be hydronephrotic—thus again emphasizing the high incidence of this condition.

He had had one interesting case of extraperitoneal rupture of the bladder complicating fractured pelvis. This was sutured and the bladder drained but unfortunately the fracture line ran into the right hip-joint and the patient developed an acute suppurative arthritis. In spite of adequate drainage of the joint and extension the patient died about six weeks later from toxæmia.

The only genito-urinary casualty from air raids was a girl of 15 who sustained a huge wound of the left hypochondrium, through which her stomach, splenic flexure and a pulped spleen were hanging out and covered with dirt. After resuscitation with 6 pints of plasma and 1 pint of blood an exploration was made, the spleen and a damaged left kidney removed, and the stomach and colon were washed and returned to the abdomen. The patient made a complete recovery in spite of losing in addition a number of ribs and sustaining a partial tear of the left leaflet of the diaphragm.

Section of Proctology

President—W. B. GABRIEL, M.S.

[*March* 12, 1941]

MEETING HELD AT ST. MARK'S HOSPITAL, LONDON

Venous Spread in Rectal Cancer

By C. E. DUKES, M.D., M.Sc., D.P.H., and H. J. R. BUSSEY, B.Sc.

The Pathology Department, St. Mark's Hospital, London

IN view of the severe consequences of the spread of rectal cancer by veins it is surprising that so little attention has been given to the state of the veins during the routine examination of pathological specimens. Our interest in this question was first aroused by Dr. P. C. Hou of Cheeloo University, North China, who demonstrated a case of cancerous occlusion of a branch of the superior hæmorrhoidal vein. Realizing the importance of such a finding we decided to make a special study of the state of the veins in rectal cancer and evolved a technique which we have now applied to 669 operation specimens.

Detection of Venous Spread

Venous spread can rarely be detected by inspecting or handling the rectum, and a dissection of the veins is usually necessary before deciding whether or not they contain malignant tissue. The following technique has been found most convenient for a vein dissection. The operation specimen is opened up along the mid-line anteriorly and sewn out on a rectangular meccano framework to preserve its natural relations. The stretched-out operation specimen is fixed in 10% formalin for twenty-four to forty-eight hours, after which the dissection can be commenced. It is best to begin with the ligated end of the superior hæmorrhoidal vessels and to work down the vessels until the terminal branches are observed to disappear through the muscle coat into the submucosa. Dissection is easy with specimens from thin patients and where there is little extrarectal spread but is more difficult in fat subjects and in cases with matted carcinomatous deposits or much inflammatory fibrosis. Bit by bit, fat and connective tissue are removed, leaving in situ veins, lymphatic glands and other deposits of carcinoma. A natural-size plan is next prepared on which all these structures are plotted. Portions of the veins, glands and extrarectal deposits are then taken for microscopic section. The most likely place to find evidence of intravascular extension is where the veins emerge from the region of the growth. Microscopic examination is always necessary to confirm the nature of any solid tissue found within the lumen of the veins. In cases where nothing suspicious has been noticed during the dissection it is seldom that any sign of venous spread is found in the sections.

Appearance of Intravascular Growth of Carcinoma

A vein containing carcinoma appears yellowish white in colour and feels hard and nodular. Only a short stretch of the vein is affected in most cases, though occasionally a solid cord is found along the whole course of the superior hæmorrhoidal vein. Often growth is found in more than one of the tributaries of the hæmorrhoidal veins and it has seemed as if some types of rectal cancer show a special predilection for extending along the veins.

The opening up of an affected vein reveals the lumen to be patent as far as the dilatation at which point the walls of the vein become stretched tightly over the solid clump of malignant tissue which occludes the lumen. As a rule the malignant tissue is not adherent to the intima. Vascular thrombosis is rare but we have occasionally found the veins to be filled with soft blood-clot entangling clumps of carcinoma cells. In most cases the malignant tissue lies free within the lumen of the vein and in direct contact with fluid blood. The ease with which fragments might become detached is at once apparent and is a warning of the danger during the operation of rough handling before the vessels have been ligated.

Widespread and massive intravascular growth is sometimes accompanied by secondary tumours elsewhere in the rectal mucous membrane: these consist of small umbilicated nodules projecting slightly from the surface. At first these are separate but they tend to become confluent later. They may be close to the primary growth or separated by several inches of normal-looking mucosa. Our dissections have shown that these secondary tumours are due to continuous growth along the superior hæmorrhoidal veins and extension to the submucous venules. This permeation of the veins, in the direction opposite to the natural flow of blood, results in the re-irruption of carcinomatous deposits in the submucosa and mucous membrane often at a considerable distance above or below the primary tumour. This peculiar manifestation of venous invasion is found only in a small proportion (about 5%) of cases in which there is evidence of intravascular growth.

The evidences of intravenous extension of carcinoma which can be found in operation specimens are more suggestive of growth along the veins by a process of permeation than of embolism, although, as already mentioned, a fragment of the growth might easily become detached and form an embolus. Support for this view is derived from the fact that intravascular spread begins at the margin of the primary tumour and pushes along the vein, bathed in the nutritious environment provided by the circulating blood. The malignant tissue grows along the vein in the same sort of way as a calculus grows down the ureter, by the constant deposition of new material at the growing "beak".

Frequency of Venous Extension

We have examined 669 operation specimens of rectal cancer by the method described and found clumps of carcinoma cells in the hæmorrhoidal veins in 111 (16·6%). In all these cases it seemed probable that venous dissemination had already taken place or would have done so in the near future. We regard this figure (16·6%) as an underestimate of the total number of cases in which venous spread was possible because it does not include those cases in which the hæmorrhoidal veins were embedded in a massive extension of the growth in the perirectal fat. We have included only those cases in which malignant tissue was found within the lumen of the veins.

Characteristic Features of Cases showing Venous Extension

Cases in which venous spread was demonstrable by dissection showed certain minor differences when compared with the general series. The average age of the 111 patients with evidence of venous spread was slightly lower than for the general series of cases of rectal cancer, the figures being 55·2 years for men and 52·7 for women. In a series of 1,000 cases of cancer of the rectum the average age for males was 58·6 years and for females 55·1 years. The lower average age of patients exhibiting venous spread was obviously related to the histological grade of the primary growth. As a general rule the higher the grade of malignancy of a rectal cancer the greater is the likelihood of venous spread. Growths of a high grade of malignancy are commoner in young subjects. Cases exhibiting venous spread are found to have a lower average age and also a higher proportion of colloid and Grade III growths (*see* Table).

PERCENTAGE DISTRIBUTION OF HISTOLOGICAL GRADES.

	Cases showing venous spread. Per cent.	Total series of 1,000 cases. Per cent.
Grade I	2·7	8·4
Grade II	37·6	55·6
Grade III	39·7	21·0
Grade IV	3·6	2·1
Colloid	16·2	12·9

Differences were also noticed in the size and position of the growths exhibiting venous spread when compared with other cases. As a general rule cases with demonstrable venous spread were large bulky tumours with obvious extrarectal extension and most commonly situated in the upper third of the rectum. But the most interesting correlation was found between the extent of spread (as measured by the A, B and C classification of rectal cancer) and the incidence of venous spread. No instance of venous spread was found in the A cases (growth limited to rectal wall) but intravascular growth was found in 35 out of 213 B cases (growth extending to extrarectal tissues but no lymphatic metastases). It was rather surprising to find evidence of venous spread in such a large number of cases without lymphatic involvement (16·4%). Amongst the 360 cases in which the lymphatic glands contained metastases (C cases) 76 were found to show venous spread, an incidence of 21·1%. The fact that there was so little difference in the incidence of venous spread in the B and C cases proves that the invasion of the veins must take place from the primary growth and not as the result of spread from lymphatic metastases.

Significance of Discovery of Growth within Veins

The full significance of the discovery of growth within veins can only be assessed when a series of cases such as these have been kept under observation for a period of five years or more. We hope that our records may answer this question more fully at a later date, but in the meantime we feel justified in saying that the discovery of growth within the hæmorrhoidal veins is not to be taken as proof of the existence of hepatic metastases. Several of our cases have been under observation for three, four and even five years and remained in good health without clinical evidence of growth within the liver. We assumed at first that whenever carcinoma was found in the hæmorrhoidal veins metastases would be found in the liver or lungs, but the results of post-mortem examinations have forced us to modify this opinion. Autopsies have been carried out in 13 of the cases where cancer cells were found in the veins and in only 3 of these were secondary deposits found in the liver. During the same period we have carried out 26 post-mortem examinations in cases where no growth was found in the veins and yet 4 of these had hepatic metastases.

Comment.—Evidence of growth within the hæmorrhoidal veins in an operation specimen is an indication that venous spread would certainly have taken place eventually if the operation had not been performed but is not to be taken as proof that spread to the liver or lungs has already occurred.

Terminal Ileostomy for Idiopathic Ulcerative Colitis.—RUPERT CORBETT, M.Ch.

This case was referred to in the discussion on surgical treatment of idiopathic ulcerative colitis in the Section in May 1940 (*Proceedings*, **33**, 647 (Sect. Proct. 11).

The patient, female, aged 28, had this operation performed just over five years ago. The onset of the disease was in September 1934. An appendicostomy was performed in December of that year. Medical treatment including numerous blood transfusions was given, but she became worse, and was bedridden, having to lie on a rubber bed-pan always. In March 1936, the terminal ileostomy was established. A dramatic recovery followed and in three months she had doubled her weight and was leading a normal life again. Now she is very fit and doing war work, and stated that she forgot she had an ileostomy. She has an unrestricted diet and takes a small amount of ferri redactum with her meals, keeping her motions dark to avoid soreness of the skin. A belt incorporating a box is worn with comfort, being emptied twice a day, morning and night. There is practically no discharge from the rectum.

Specimens Shown:

Dr. CUTHBERT DUKES and Mr. H. J. R. BUSSEY: **"Venous Spread of Carcinoma of the Rectum."**

Professor G. GREY TURNER: **Specimens of Cancer of the Rectum.**

Mr. O. V. LLOYD-DAVIES: **Specimen of Squamous-cell Metaplasia.**

Short Films:

Mr. W. B. GABRIEL: (1) **Excision of Anal Fissure.** (2) **Diffuse Cavernous Angioma of the Pelvic Colon and Rectum.**

Demonstration:

"Surging Faradism for the Treatment of Sphincter Relaxation."

Cases:

Mr. LIONEL E. C. NORBURY: **Ulcerative Colitis. Paul's Operation.**

Mr. C. NAUNTON MORGAN: **Gas Gangrene Infection. Tuberculous Fistula. Lymphogranuloma. Nerve Division. Amputation for Prolapse.**

Mr. O. V. LLOYD-DAVIES: **Abdomino-anal Excision. Tuberculous Fistula. Tuberculous Recto-vaginal Fistula. Lipoma of Rectum.**

Mr. W. B. GABRIEL: **Anal Ulcer: Case for Diagnosis.. Lymphogranuloma. Tuberculide of Anus.**

Section of Otology

President—LIONEL COLLEDGE, F.R.C.S.

[*March* 7, 1941]

DISCUSSION ON THE LIMITATIONS OF OPERATIVE TREATMENT IN TRAUMATIC FACIAL PARALYSIS

Miss D. J. Collier: Injury to the facial nerve in the mastoid operation is an uncommon complication but the result is so disastrous that an inquiry into the best available method of treatment needs no justification. Though this discussion is limited to facial paralysis of traumatic origin in order to exclude the more controversial subject of Bell's palsy, it is not out of place to note that the lines of treatment suitable for traumatic palsy are applicable also to the rare cases where the continuity of the facial nerve has been lost from the erosion of an intratemporal epidermoid, or from a perineural fibroblastoma occurring in the neighbourhood of the fallopian canal.

When the facial nerve is damaged in the mastoid operation, conductivity may be lost either by pressure from outside which prevents the passage of the nervous impulse, or there may be complete interference with continuity by section of the nerve, or actual loss of substance. The pathological factor in the compression injuries may be simple œdema or hæmorrhage with an intact sheath, or a torn sheath, or pressure by detached bone from fractures of the wall of the fallopian canal. I have found all these conditions at operation. Exploration alone can determine whether the nerve has been divided or merely compressed, and should be undertaken if, in the third week after onset of the paralysis, examination under general anæsthesia shows the reaction of degeneration and absence of the faradic response.

Operative damage to the facial nerve may involve the segment in the petrous bone, e.g. from the removal of a sequestrum of the labyrinth; it may be isolated in the middle ear, at the bend below the external semicircular canal, or in the descending portion.

Colledge (1936) referred to the importance of distinguishing between cases in which the tympanum was intact, and those in which it had been destroyed by a radical operation, and questioned whether the operator was justified in destroying an intact middle ear, or risking it with the rather equivocal prospect of correcting the facial palsy. In my operative experience of patients with injury to the facial nerve from the mastoid operation involving, it is true, only 19 cases, I have never found damage isolated in the middle ear after a cortical operation; where a graft has been necessary to replace nerve damaged in the middle ear and at the bend below the external canal, the integrity of the middle ear has already been lost. Injury to the facial nerve in an operation that leaves the middle ear intact is likely to occur only in the vertical portion where the nerve may be damaged when opening the chain of cells behind the posterior meatal wall. Exploration in these cases should be done from below at the stylomastoid foramen when the vertical portion of the fallopian canal can be exposed, and the nerve decompressed or grafted without damaging the tympanic membrane or the middle ear, leaving the patient with an intact middle ear and normal hearing.

There are special features present in the facial musculature which may interfere with the restoration of perfect function—i.e. "with the manifold delicate shades of facial expression resulting from varied emotional reactions". In the first place, unlike the skeletal muscles which are bound into compact muscle bundles by fascial tissue, there is

no definite muscle fascia surrounding individual facial muscles. As a consequence, smaller muscle portions may contract independently of the rest of the muscle in varied contractions with synergic muscle portions within functional muscle groups. Associated with this arrangement is the absence of superficial fascia, although the neck portion of platysma is covered by a thin sheet of such fascia. This is not surprising, as a veil-like covering of fascia spread over the thin and delicate muscles would make elaborate facial expression impossible. Without superficial fascia the muscles lie directly under the freely movable skin where they are inserted in the subcutaneous tissue or firmly attached to the skin itself. The attachment to the skin is particularly noticeable in the superciliary region, in the naso-labial fold and over the chin. When these muscles contract the elastic skin goes into folds which are generally at right angles to the direction of the muscle bundles. When the muscles are inserted directly into the skin contraction produces grooves or dimples. "Individual muscle variations, differences in thickness of the skin and subcutaneous tissue and differences in the elasticity of the skin naturally have modifying influences, thus adding to the individuality of facial expression." The rich branching of the facial nerve after it leaves the stylomastoid foramen affords the necessary motor innervation to the varied muscle groups. Deep sensibility from the face—deep skin and muscle pressure—is carried in the 7th and not in the 5th nerve. Harvey Cushing from observations after section of the sensory root of the 5th nerve concluded that true muscle sense—i.e. proprioceptive sensibility—is transmitted through the 5th nerve, but Ernst Huber (1930) of Johns Hopkins Hospital, to whose work on the facial musculature I am much indebted, found from experimental studies that muscle sensation from the mimetic musculature is conducted, together with muscle pressure sensibility, by the branches of the 7th nerve.

I have noted in every case of recovering function after either decompression or nerve graft that the patient acknowledges the presence of local sensations in the muscles which they find difficult to describe other than by saying they think the muscles are moving. These occur at varied intervals before any muscular contractions are visible. Specific sensory organs in the facial muscles corresponding to the muscle bundles of the rest of the voluntary musculature have not yet been described. It is probable in normal circumstances in addition to the direct appreciation of muscle contraction with the aid of muscle sense through the 7th nerve, that postural sensations are carried back through the 5th nerve from the skin when the latter is under tension and wrinkled through the contracting facial muscles.

As power cannot be restored to muscles which have undergone fibrous atrophy, absence of galvanic response is a contra-indication to any operative treatment directed to the nerve supply. What is perhaps less well appreciated is the possibility that fibrosis may involve parts of the small muscle bundles of the facial musculature interfering with that synergic contraction within the larger functional muscle groups that gives rise to the infinite variety of expressive movements. This fibrosis may also be responsible for the non-return of movement to the frontalis muscle after the graft operation; i.e. in cases where the muscle is necessarily denervated for a relatively long time, in contrast to the early return of movement in this muscle in cases which recover without interference.

The quality of the result will also be influenced adversely if the muscles have been allowed to stretch during the period they are denervated. This can be prevented to a limited extent in the muscles around the mouth by using a hook or splint in the angle of the mouth. The movements of the normal side can then no longer pull the lips across the mid-line and thus stretch the paralysed muscles. External splinting by means of elastoplast is useful especially for the elevators of the upper lip and side of the nose.

Massage which maintains the nutrition of the muscles and supports the patient's morale, should be directed to preventing elongation of the muscles. One patient whose recovery is the most satisfactory I have yet achieved, had his after-treatment carried out by his mother, a trained beauty specialist experienced in those massage manœuvres aimed against sagging of the facial muscles.

Regressive alterations occurring in the end organs in denervated muscles may interfere with the return of function even when continuity of the nerve is restored.

The changes that occur in the nerve cell consequent on section of the axon are at first reversible. Presumably there is a time limit to this, but we know very little about the persistence of regenerative power in the central end of a divided nerve. Anatomically the central end must be accessible if a graft is to be employed. The central end was

missing in three of my patients; in one removal of a sequestrum of the labyrinth which must have involved most of the inner ear and internal auditory meatus had left exposed the dura mater of the middle and posterior fossæ. The central end was missing and the graft operation had to be abandoned. In two others, one following operative treatment for meningitis, I failed to find a central end. Dr. Tickle (1938) who worked with Duel has reported successful grafting in a case where removal of a sequestrum after necrosis of the labyrinth had left a neuroma on the central end of the nerve, just outside the dura mater.

If the peripheral end of the facial nerve is in the soft tissues outside the stylomastoid foramen (this may occur when the nerve has been injured in infants), it is necessary to suture the distal end of the graft to the nerve. In two patients, not infants, where I found the lower end in the soft tissues I failed to get any return of muscular movement. Probably excess of endoneural scar, due to the sutures, was responsible. These cases are very rare, but if I meet one again I shall use the plasma method.

Leriche (1940) maintains that failure of regeneration after suture of peripheral nerves is due to ischæmia, produced by stripping the nerve ends from their bed above and below the lesion, so destroying their fine vascular supply. He considered that the environment in which the injured nerve lies has a great influence on its chance of successful regeneration. Leriche explains the better results obtained in suture of the musculospiral nerve than with the median and ulnar nerves by the fact that it lies free in a vascular bed. This would seem to suggest that the avascular bony channel of the fallopian canal offers a most unfavourable bed for a nerve graft. It is, however, probable that a nerve graft is vascularized along its course from end to end, and not laterally from its bed to any extent. In the fallopian canal, the stylomastoid artery entering at the foramen and the superior petrosal artery entering at the hiatus fallopii provide an effective blood supply.

I consider that nerve grafting in the temporal bone owes its success to the presence of the rigid bony channel in which the inlay can be maintained without the necessity for sutures. All the experimental and histological work on nerve grafting, particularly that of Bentley and Hill (1936) and the work at Oxford of Young and his associates (1940 (*a*), (*b*)) has established the importance of minimizing endoneural scar formation at the two junctions of graft and nerve. If this scar formation is at all extensive it forms an inevitable barrier to the downgrowth of regenerating axons. Minimal formation of scar tissue is ensured by accurate approximation of nerve and graft. This requires a graft equal in calibre to the recipient, which for the facial nerve can be supplied by the middle cutaneous nerve of the thigh. The fixed ends of the nerve and the graft must be cut accurately at right angles to their long axis to secure perfect apposition. This is more easily done with the degenerated graft, and may be responsible for the good results Duel claimed for these grafts. In five patients I have found such destruction of the bone around the area where the nerve substance had been lost that there was no fallopian canal in which to lay the graft. There has been no restoration of function in any of these cases, which can be accounted for by the fact that accurate contact between graft and nerve could not be maintained. Since seeing the work with plasma suture at Oxford, I am confident that absence of the fallopian canal will not in the future constitute an obstacle to successful operation, as by this method the nerve and graft can be securely stuck together with the minimum of endoneural scar formation.

It will be obvious that, granted continuity of the nerve can be restored, the factor most likely to influence the chance of successful conduction of the nerve impulse to the end organs is the length of time the muscles have been denervated. Here the absence of an absolute test on which to base prognosis in the presence of traumatic facial paralysis is most serious. This time factor is more important in the thin delicate muscles of facial expression than in the muscles of the limbs, even in the small muscles of the hands. To wait for spontaneous recovery without an adequate basis for hope is likely to be more disastrous in the facial than in the peripheral nerves.

In gunshot wounds of the limbs experience in the last war showed that operation on the nerves before six months have elapsed, would often lead to unnecessary operations, as the damage is more often due to bruising or other reversible process, than to actual division of the nerve. A period of observation up to this limit did not apparently interfere with the success of surgical treatment if this became necessary from absence of any sign of regeneration. The situation in the temporal bone is not comparable. Here the nerve is enclosed in a bony canal, which it completely fills and to which its sheath is firmly

attached. The vascular changes that follow trauma of the nerve are responsible for the compression of the nerve elements. Apart from actual section of the nerve, I believe tearing of the nerve sheath which increases the initial hæmorrhage into the fallopian canal adds to the compression. In advocating early operation in those cases where the faradic response is absent under an anæsthetic and the reaction of degeneration is present, I am perhaps influenced by my own operative experience. This is limited to 19 cases but in 14 of these the facial nerve was severed, and in 4 others the nerve sheath was torn.

The surgeons who advocate nerve grafting for accessible lesions of the facial nerve with loss of continuity, claim that it is a better physiological proceeding than nerve anastomosis in that it aims at restoring the pathway between the motor cortex and the muscles for which the cortical impulses were originally intended. The passage of time and follow-up of patients have shown that the degree of recovery obtained is far from perfect. In assessing the results of restoration of function to one side of the face we have to consider the importance of symmetry. This requires a standard of perfection necessarily high.

Limitation of functional recovery after a successful operation on the facial nerve, that is, one in which the nerve conducts impulses across a segment where Wallerian degeneration had previously taken place, may be due to weakness of individual facial muscles with consequent failure in symmetrical movement. It may also be due to abnormality of movement producing tics or isolated, purposeless, contractions of individual muscles or muscle groups, while at the same time synkinesia or mass movements may be a prominent feature of every facial movement, volitional or emotional. So-called "contractures" of the facial muscles producing deepening of the naso-labial fold and narrowing of the palpebral fissure as compared with the normal side may interfere with the symmetry of the final result. In all my nerve graft patients, weakness in action of some of the facial movements has been present. Failure in recovery of the frontalis does not give me much anxiety as the effect on the æsthetic or cosmetic result is not unattractive. Weakness of the elevators of the angle of the mouth, the upper lip and side of the nose is more important. It is present in most cases and, as I said earlier, it may be due to overstretching of the appropriate muscles during the time they are denervated.

Much has been written about the facial tics that accompany restoration of movement after complete degeneration of the nerve. Ballance and Duel (1932) noted these isolated muscle twitches in their experimental work, and Duel (1933) commented on their occurrence in the post-operative state of his nerve graft patients (Fowler, 1939). They disagreed, however, on the factors responsible; Ballance believed the facial myoclonus had a central origin—that it was an irritative phenomenon due to tissue and vascular reactions around the degenerating nerve cells of the facial nucleus in the medulla, and Sullivan (1936) in Toronto supports this view. The evidence, histological and experimental, produced in the research initiated by Duel in association with Howe and Tower (1937) at Johns Hopkins Hospital confirms the peripheral origin of the tics and the mass movements. These workers demonstrated the presence of branching axons at the point of trauma in the regenerated facial nerve, and showed physiologically that branches of one axon may be distributed to innervate widely separated parts of the facial musculature, bringing about a permanent functional union between muscles which do not normally contract simultaneously. In this way the purposive innervation of one part of the facial musculature is accompanied by an involuntary mass contraction of the rest of the face. It was noted that the adventitious movements about the mouth were always synchronous with some purposeful facial movement—e.g. the involuntary blinking of the eyelids—and they are believed to depend on a phenomenon similar to the axon reflex, due to branching of axons at the site of degeneration. This diffuse distribution of the regenerated nerve fibres, may produce excessive stimulation of all the facial muscles which keeps them in a state of hypertonicity, thus leading to contractures.

Mass movements may also be due to the excess of neurofibrils which occurs in the peripheral stump after regeneration. This may be Nature's way of increasing the chance that some fibres will take the correct path and become ultimately the functional axis cylinder.

Facial tics or isolated purposeless movements are most commonly present in the muscles of the chin and from their continuous presence and the attachment of the involved muscles to the skin they lead to contractures that may show as dimples. Most

patients are not aware of these isolated contractures even on close questioning, and the few who were conscious of the twitches were not disturbed by them.

Some degree of synkinesia has been noted in all my graft patients, but I do not agree with the American critic who says: "the entire facial musculature on the affected side is made a single functional unit and with every movement the facial muscles move *en masse*" (Coleman, 1940). When the patient closes his eyes there is only the slightest movement of the angle of the mouth on the affected side, sometimes scarcely perceptible. Certainly there is no grimace-like movement of the whole face. Careful examination shows that varied isolated movements are possible, both emotional and voluntary.

In discussing the mass movements that accompany restoration of function to the facial nerve it is interesting to note that the range of isolated facial movements varies in different individuals. Darwin (1890) pointed out that some short-sighted people, who contract their orbicularis oculi when looking at distant objects, raise the upper lip at the same time. This gives them an habitual, grimacing expression. The contraction of additional muscles when movement of a limited group is intended, is shown in other individuals who cannot contract the superciliary muscles without at the same time tightly closing their eyes with the orbicularis oculi. This phenomenon is presumably a persistence of a phylogenetically older, less differentiated pattern. Through special effort and with continued practice such persons may succeed in eliminating the associated movements as is ordinarily done in frowning. We may assume that through such a process of gradual functional perfection, finely graded facial expression has evolved from a lower stage where crude grimace-like group action prevailed, as in the anthropoid apes and the lower primates.

Although there is complete structural differentiation in the facial muscles and corresponding branches of the facial nerve at birth, there is practically no facial expression in the newborn. Expression evolves gradually with the elaboration of association centres. At first emotional reactions are uncontrolled, but with increasing experience, and under the influence of education, emotional impulses which in the child would cause spontaneous response in the facial field, are counteracted or modified by a complex association mechanism (Huber, 1930).

It should be the aim of the physiotherapist to train these patients while power is returning to the facial muscles. The muscles of the sound side must be relaxed while the patient practises before a mirror the movements he must relearn. It is particularly important at this stage to prevent strong movements of the normal side from pulling against the weak recovering muscles. An impassive face should be cultivated. Synkinesia and overactivity of muscle contraction is more pronounced when the patient is under emotional stress. For instance, one girl appeared to be developing contractures when she was working for an examination, but when this period of strain was over her facial movements became more normal. This seems to indicate that some overactivity may be due to diffusion of the numerous stimuli which play on the face muscles in such circumstances. Further evidence that cortical control may modify the results of axis branching or misdirection of nerve fibres is supplied by Ballance's observation that the facial twitch noted in experimental animals after recovery of the facial nerve became more pronounced under light anæsthesia when control of the higher centres is cut out (1934).

We are still far from understanding the total mechanism involved in facial expression and the influence which the cortical centres can exert on facial movements either by way of initiation or inhibition. I recall one patient seen first many years after a mastoid operation, which had left her with apparently complete facial paralysis. She had absolutely no spontaneous facial movements, but she could make good voluntary contractions of the muscles about the mouth and eyes: a dissociation of facial movement the anatomical basis of which I am unable to interpret.

After examining my post-operative films Professor Cave of the College of Surgeons, noted that weakness of the infra-orbital muscle sheet, represented chiefly by levator anguli oris and levator labii superioris, seems responsible for most of the expressional deformity. He agreed with me that it is possible that atrophy of the very slender muscle bundles is never completely recovered from. But on purely morphological grounds he thought that this specialized part of the facial musculature is likely *a priori* to recover less after facial paralysis than the more primitive sphincteric mass around the eyelids and lips, as it is precisely in this infra-orbital facial area that evolutionary processes are still at work. The older sphincters of the lids and lips are morphologically fixed and static and

they appear to recover remarkably well; the phylogenetically more recent infra-orbital sheet does not do so well and it is on this plastic, mimetic, infra-orbital musculature, that normal facial expression depends.

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Mr. J. Z. Young (*abstract*): The rate of growth of nerve fibres through fresh and pre-degenerated autografts has been measured directly in the rabbit by finding the distance reached by outgrowing fibres after fifteen and twenty-five days. No appreciable differences between the two types of graft were found and any advantage of the pre-degenerated grafts must therefore be due to other factors such as consistency and ease of manipulation.

The actual rates of growth observed were little less than through a normal peripheral stump, and there was no evidence of great delay at the more distal end of the graft. At least with thin grafts revascularization takes place within a few days and there is no necrosis at the centre of the graft. New fibres entering a graft rapidly become medullated. These experiments therefore confirm those of others in showing the possibility of the establishment of good nervous connexions by means of grafts.

The placing of facial grafts might be considerably assisted by the use of the concentrated plasma solutions described by Medawar and Young (1940, *Lancet* (ii), 126), which have been used with great success for grafts in animals. The plasma serves to hold the graft in place and to hold the junctions together. It might also be used to make a support for the graft if the bone is damaged, since it sets to a rigid gel of firm consistency.

Dr. F. S. Cooksey: The normal facial nerve will conduct the faradic current and cause a tetanic contraction of the corresponding facial muscles. If a proportion of the axons have degenerated a stronger faradic current is necessary to produce a minimal contraction, and the increase of current required is an approximate indication of the extent of degeneration present. When all the axons are degenerated the power to conduct the faradic current is lost.

The response of the normal muscle and nerve to the interrupted galvanic current is a brisk twitch at each interruption of the circuit. When the lower motor neuron has degenerated the nerve is non-excitable and the muscle fibres respond by the so-called sluggish reaction, the characteristic feature of which is a much prolonged relaxation after each contraction. When degeneration is present less galvanic current than normal is required; and, on account of this hyperexcitability, the sluggish reaction will appear as soon as quite a small proportion of neurons have degenerated. Thus the only significance of a sluggish galvanic response is an indication that an indefinite number of axons have degenerated.

Usually the electrical changes of reaction of degeneration do not appear before ten days after the injury, and are not reliable before the fourteenth day.

At clinical examination failure of the nerve to respond to the full strength of the faradic coil together with the sluggish galvanic response in the muscle may be taken as strong evidence that reaction of degeneration is complete. But in some cases due to an unduly high skin resistance a faradic response may not be obtained, and yet when the nerve is exposed at operation and an electrode applied directly to the nerve conductivity can be demonstrated; for this reason the nerve should be stimulated at operation unless it is

obvious that continuity is lost. Some patients will not tolerate sufficient faradic current for adequate clinical examination; but the difficulty can be overcome by repeating the examination under an anæsthetic such as pentothal.

The electrical reactions may be used as a guide to regeneration; but in this connexion they are of limited use since voluntary power usually returns some weeks in advance of return of faradic response. Nevertheless, over long periods the electrical reactions show whether the nerve conductivity is improving or not and, at times, may be useful in demonstrating that failure to recover voluntary power is due to inadequate re-education or functional causes.

Physical methods are used in the after-treatment of nearly all operations for facial nerve paralysis. There are two stages and distinction between the two is important. Firstly, there is the period of complete paralysis which lasts until the regenerating axon reaches the motor end-plate and, secondly, the stage of recovery which begins with the first flicker of returning voluntary power.

In the first stage, treatment is directed to maintaining the condition of the muscles in as favourable a state as possible for ultimate recovery; for this splints, massage, and galvanism are the established practice. It is a waste of time to attempt re-education in this stage since it is physiologically impossible for voluntary movement to be obtained. Unfortunately it is a common mistake to attempt re-education too early with resulting distress to the patient who sees no reward for weeks of treatment and the constant effort leads to overaction of the unaffected side of the face to the detriment of the final result.

The use of galvanic stimulation of the paralysed muscles is open to criticism, and recent experimental evidence has suggested that it may be actually harmful to the muscles and delay recovery. Certainly it can be detrimental if many and strong contractions are given. It should be used to produce some ten gentle contractions of each muscle daily and used in this way it does seem to maintain the excitability of the muscle fibres and power of ultimate recovery longer than in those cases which have not had the treatment. When circumstances are favourable for rapid regeneration galvanism is unnecessary, but the majority of cases on which operations are performed are of long duration and regeneration is slow. All that can be said is that the consensus of clinical opinion is in favour of the use of galvanism, more especially in long-standing cases.

In the stage of recovery patient re-education is of paramount importance and massage and electrical treatment are of diminishing value. Regular treatment at this stage is essential, and the patient must be impressed with the need of regular practice of movements at least four times daily in front of a mirror at home. Although the importance of re-education is obvious and calls for the maximum effort from the patient and masseuse, it is common to find treatment neglected at this stage, usually because the patience and hope of the patient are exhausted. For this reason it is advisable to restrict treatment in the stage of paralysis to the minimum which will maintain the excitability of the muscles and prevent deformity. When recovery is slow two weeks' daily treatment every two months is more effective than continuous treatment once or twice a week. Treatment should be sustained for three months after the onset of recovery and thereafter there should be a short course at regular intervals; otherwise the patient is liable to lose interest and concentration.

It is always difficult to know when to abandon hope of further improvement. Recovery may continue for three or four years after nerve grafting; but usually the maximum is reached in two years. After facial nerve grafting or anastomosis with the hypoglossal nerve, complete dissociation of facial movement is seldom obtained. The return of tone to the muscles gives a good cosmetic result when the face is at rest and in ordinary quiet conversation; but sudden expression of the emotions causes mass movements of the muscles on the affected side and rather distressing grimacing. Prolonged attempts at re-education are liable to accentuate the range of movement on the normal side and to increase the mass movement and grimacing on the affected side. It seems better to train the patient to restrict the range of movement on the normal side; that is, to cultivate a "poker face", so that the normal muscles are trained to restrict movement to match the best that can be obtained on the paralysed side.

In the later stages of recovery the affected muscles are liable to develop excessive tone, leading to overcorrection at rest and even to involuntary tonic and clonic contractions. This is usually due to the prolonged use of electrical stimulation after the return of moderate voluntary power. Electrical treatment should be discontinued immediately this

complication is seen. The increased tone usually disappears a few weeks later; but it may persist, and for this reason it is of some importance to discontinue electrical stimulation just before the tone of the recovering muscles approaches that of the normal side.

Mr. Terence Cawthorne: The object of surgery in the treatment of traumatic facial paralysis is to encourage the downgrowth of healthy nerve fibres through the degenerated nerve trunk to the motor end-plates of the facial muscles. This was formerly accomplished by anastomosing the degenerated end of the nerve to a nearby motor nerve in the neck, but the work of Ballance and Duel, Bunnell, Martin and others has shown that the best results are to be expected if the healthy end of the facial nerve itself is used to supply the active nerve fibres. To do this they advocate exposing the nerve at the site of injury and joining the two ends either directly or by the interposition of an autogenous nerve graft.

The restoration of movement following a nerve graft operation takes some time and it is not always easy to make a patient appreciate that the operation is not analogous to the joining up of the broken ends of an electrical circuit in which, as soon as the join is effected, the current flows.

There is, as a rule, no difficulty in restoring facial movements in suitable cases; in fact rather the reverse is not infrequently noted. Movements are exaggerated and it may be difficult to obtain dissociated action of individual muscle groups. This exaggerated action and mass movement following recovery is the principal limitation to success and may in part be accounted for by the fact that only a proportion of the active nerve fibres find their way down into the degenerated nerve. The formation of fibrous tissue undoubtedly plays a large part in hindering the downgrowth of new nerve fibres.

In an experimental study of joining divided nerves Bentley found that inaccurate apposition of divided nerve ends, and the introduction of sutures, provoked a marked fibrous tissue reaction, the degree of which was in proportion to the inaccuracy of the apposition and the size of the sutures. Sutures should, if possible, be avoided and of course so far as the intratemporal part of the facial nerve is concerned sutures are not necessary. Outside the skull if sutures are required I have been in favour of anchoring sutures at some distance from the actual junction of the two ends, but I think that the concentrated plasma solution may obviate the necessity for any suture.

Another important factor in minimizing fibrous tissue formation is the degree of accuracy with which the nerve ends are joined together and in order to ensure accuracy of apposition of nerve ends or nerve grafts I have for some time been in the habit of using a dissecting microscope for facial nerve operations. I have found that with the magnification obtained it is easier to be sure of accurate apposition.

The possibility of using the dissecting microscope for the operations suggested itself to me after I had seen Professor Dohlman's work at Lund and Mr. C. S. Hallpike also suggested that it might be used for certain operations on the labyrinth; we have used the microscope for labyrinth operations since the autumn of 1938. Also since then I have found it of the greatest help in recognizing details of the facial nerve and in ensuring accuracy of apposition of divided ends.

When using grafts I have felt that it is wiser to delay operation until the site of injury is clean, so that when the graft is inserted, it can be covered by muscle, turning down a flap if necessary. I think that operating in the presence of sepsis may increase the fibrous tissue reaction, and the use of gold leaf to cover the grafted area may also favour fibrosis, although I have seen good results even when the grafting has been carried out in a septic area.

I cannot say whether end-to-end anastomosis gives better results than nerve grafting because with but one exception I have always found that in cases of complete division the gap that is left after the ends have been properly trimmed is too great to be bridged without a graft, even after mobilizing the lower end. I have on two occasions met with cases of fairly long-standing paralysis in which the continuity of the nerve was intact but at the site of injury was a swelling which I excised, bridging the gap with a graft, and facial movements were eventually restored. In one of these cases the swelling proved to be a neurofibroma.

No matter how complete the repair of the facial nerve may be, movements will only return if the muscles are active. Therefore, the success of any operation will depend upon the state of the facial musculature, and this will be governed by the way in which the muscles have been treated during the period of paralysis. Provided that they have

been properly supported and that their nutrition has been maintained by suitable exercises I do not think that the final result will be jeopardized by a few weeks', or even months' delay. I mention this because it is often necessary to wait for some weeks until the sepsis has been cleared up. During the early stages of paralysis it is important to prevent overstretching of paralysed muscles and patients should be urged to wear some form of support. Gillies has suggested that the surest way of preventing overstretching would be to insert a temporary fascial sling. During the period of paralysis treatment to maintain proper nutrition of the muscles will be required, and I believe that massage with possibly occasional periods of gentle galvanic stimulation are desirable. As soon as voluntary movement returns, re-education of facial movements should be instituted and this forms a very important part of the management of these cases. Much can be done with re-education in a co-operative patient to overcome the exaggerated movements and I doubt whether this aspect of the management of these cases receives the attention it deserves, especially from the patient.

In neglected cases there may be little or no active muscular tissue in the face and it will then be useless to attempt any operation on the nerve. Instead the operation of Gillies which he described at a Summer Meeting of this Section in 1934 will give a certain amount of facial movement.

I think that the principal limitation of the operative treatment of facial paralysis is the difficulty in overcoming exaggerated and mass movements. Careful re-education, the restoration of continuity of the facial nerve wherever possible and, in the surgical technique, the avoidance of anything that may favour fibrous tissue formation are the principal means of ensuring a good result.

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Mr. A. Dickson Wright referred to a film showing some results of facial hypoglossal nerve anastomosis, especially in children; one child, now 14 years of age, had powers of expression on the side on which facial hypoglossal anastomosis had been done. In the enthusiasm for this new method of grafting, which was a definite advance in surgery, some cases might be let drift into permanent paralysis in the group of failures which Miss Collier described. He felt that all those cases should have had facial hypoglossal anastomosis done after a hundred per cent. grafting failure, although this operation should not shut the door to some form of nerve grafting. In a recent case in which he carried out facial hypoglossal anastomosis, he used half the nerve for the purpose and brought the other half up to the proximal end of the facial nerve. Later, if some movements returned to the tongue, it might be justifiable to re-operate to restore the facial nerve. He differed from some of the speakers on the meaning of "tic". A tic was a complex movement the patient could make of his own volition and these so-called "tics" in the facial muscle after operation did not come into that group because the patient made movements which he could not make voluntarily. Some of the chronic types, for instance, got clicking in the ears and noisy movements in the throat from the movement of the stapedius and digastric; and one felt that it was a condition of clonic facial spasm in which the whole nerve was at fault and had nothing to do with the centres of the brain. Some cases of clonic facial spasm develop after facial nerve injuries and sutures and he had performed facial hypoglossal anastomosis in some of these cases. In other cases he had adapted a Stöffel's operation, dissecting the facial nerve through the parotid gland. He had thought that this would be extremely difficult but found he was able to operate under local anæthesia and get into the smaller branches, removing a few of them and thus reducing facial movements.

As to after-care he recommended a pensive attitude when reading or writing, with the paralysed cheek supported by the hand; and he had the bed raised on blocks as the muscles sagged far more when the patient was sleeping than when awake.

Mr. Young's discovery of concentrated plasma was something for which the whole profession would be indebted to him and he (the speaker) had used something rather like it for some time. He found that after defribinating plasma to procure serum there was

left in the centre a considerable mass of fibrin. This was removed and ironed out into a sheet and by wrapping up the severed nerve in this the ends could be held together without sutures. The adhesion was surprisingly firm and no sutures were required. Much of this fibrin was being poured away at the present time. He used it in another way. Mr. Cawthorne had mentioned the use of gold leaf, but the speaker used the fibrin to cover up the whole of the mastoid cavity after operation. It could be used in any thickness. Another advantage was that it was a most efficient styptic. For instance, when a bone structure was oozing and full of blood clot, the fibrin was pressed in, glued itself to the bone and all oozing immediately ceased.

Section of Epidemiology and State Medicine

President—J. ALISON GLOVER, O.B.E., M.D.

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Factors Influencing the Prevalence of Trichinosis in Man

By PAUL B. BEESON, M.D.

American Red Cross—Harvard Field Hospital Unit

MECHANISM OF INFECTION

TRICHINOSIS is acquired in only one way: by eating meat which contains living larvæ of the nematode, *Trichina spiralis*. Prenatal transmission does not occur; nor is infection conveyed by excreta. The cycle of the parasite, essentially the same in all hosts, is briefly as follows: during the digestion of infected meat, Trichina larvæ are set free in the intestine, where they mature within a few days, and mate. The females burrow into the wall of the intestine and deposit their larvæ there. The larvæ enter blood-vessels and are carried in the blood to all parts of the body. (The adult females and males are gradually excreted in the fæces.) As the larvæ grow they become too large to pass through capillaries, and are therefore arrested in various organs. Those which lodge in voluntary muscle may become encysted and remain alive for many years. Those which are arrested in other organs stimulate an acute inflammatory reaction and are usually destroyed within a few weeks.

ILLNESS ASSOCIATED WITH TRICHINOSIS

Illness of the host occurs only during the period of invasion by the parasite. Subsequently the host apparently suffers no adverse effect from the presence of encysted larvæ in his muscles. As usually described, the illness caused by trichinosis has four cardinal features: fever, orbital œdema, myalgia and eosinophilia. Many other signs and symptoms may occur, depending on chance deposition of parasites in various parts of the body. Inflammatory reactions in the brain, lungs or heart may give rise to clinical signs suggestive of encephalitis, pneumonia or myocarditis. Trichinosis is rarely fatal; recovery usually begins within three weeks of the time of onset of symptoms. Some muscular stiffness and weakness may persist for several weeks or months, but complete recovery is the rule, even though the muscles are heavily infested with live parasites.

A striking characteristic of trichinosis is variation in severity of illness in different persons. All degrees of severity are observed, from fatal illness to slight indisposition, and some infestations probably occur without causing any subjective disturbance in the host. Two important factors which influence the severity of illness are the size of the infecting dose and the resistance which the host offers to the parasite.

The size of the infecting dose has a direct effect on the severity of the illness. This is natural, since the causal agent of trichinosis, unlike a bacterium or a virus, does not multiply within the body of a host. In experimental animals it is possible to determine the number of parasites which may be expected to cause death of the host. Smaller numbers of parasites cause illnesses of varying severity corresponding roughly with the actual numbers (Roth, 1939*a*).

The reaction of the host to invasion by Trichinæ may be influenced by either natural or acquired resistance to the parasite. Among persons or animals not previously exposed to trichinosis there appears to be marked variation in natural susceptibility to illness. For

example, in most of the reported epidemics of human trichinosis the number of persons who have been ill has been less than half the number of persons known to have been exposed to infection. The following example, observed in one of the recent epidemics in England, is typical: six persons ate approximately equal amounts of pork sausage. In the succeeding period, four of the six persons remained well; the fifth had a mild illness of four days' duration; while the sixth person was seriously ill for three weeks, with the classical syndrome of trichinosis. Children as a group have a natural immunity to the disease.

In addition to natural resistance, some degree of active immunity is developed after one infestation. Experimental animals which previously have been invaded by the parasite will survive infecting doses which are fatal to control animals (Roth, 1939*b*; McCoy, 1931). In human beings there have been few verified instances of recurrent clinical trichinosis (Kaufman, 1940). The mechanism of this acquired immunity is not clearly defined. It is known, however, that specific antibodies appear in the blood of persons or animals after an infestation (Bachman, 1928).

Clinical diagnosis of trichinosis is often difficult, particularly in mild cases. Two practical methods of case-finding may be used: the differential leucocyte count and the skin test with Trichina antigen (Barrett and Sears, 1938; Ferenbaugh, Segal and Schulze, 1938; Warren, Drake and Hawkes, 1935). When the differential leucocyte count is employed, eosinophilia is regarded as an indication of trichinosis, if other causes for eosinophilia can reasonably be excluded. This is a fairly reliable means of case-finding within three months of the time of supposed infestation. The skin test with Trichina antigen is a more specific method, and is simpler in practice. It can be done anywhere, and the result is obtained while the subject is available for questioning. The test material is a saline suspension of powdered larvæ of the parasite; this is injected intradermally. A positive reaction, which consists of wheal and erythema, appears within fifteen minutes. Such a reaction can be elicited in nearly all persons for at least six months after infestation. Recently the writer, with Col. C. Maddock of the Ministry of Health, performed skin tests on a number of persons residing in parts of England where trichinosis had been prevalent.[1] Every one of twenty-two persons who had suffered illness typical of trichinosis within the preceding three or four months exhibited a positive reaction. In addition, eighty persons, not known to have had the disease, were tested. In this group twelve positive reactions occurred. These twelve persons were questioned in regard to recent illness, and nine stated that they had been ill during the period when trichinosis had been prevalent in their community. Their symptoms, though not as distinctive as those of "typical" cases, were compatible with a diagnosis of trichinosis. Only two in this group remembered having had puffiness of the eyelids. Most of them mentioned backache, fatigue and low fever. The remaining three positive reactions may have signified infestation at some previous time, or these individuals may have undergone a recent infestation without having had any symptoms. Additional field studies of this type should furnish useful information on the incidence and character of mild cases of clinical trichinosis.

Examination of muscles obtained at autopsy is the best means of determining the incidence of trichinosis in a given population. In the United States, studies of this type have revealed that the incidence of trichinosis varies from 3% to more than 20% of the population, the average being about 12%. On the basis of this it may be inferred that several millions of persons in the United States are now infested with *Trichina spiralis*, and, on the same basis, that many thousands of infestations are occurring there every year. This is far greater than the number of cases of trichinosis recognized clinically. The average number of cases of trichinosis reported in States which contain two-thirds of the total population is less than 500 per year (Sawitz, 1938). Cases of trichinosis are seen only occasionally in any large American hospital.

The disparity between the incidence of trichinosis in the people of the United States and the number of cases in which a clinical diagnosis is being made indicates that some revision of former concepts is desirable. The syndrome which has been thought to be typical of clinical trichinosis probably occurs in a very small proportion of persons who become infested, namely the severest cases. Many persons who contract trichinosis have less distinctive symptoms and signs, and in these cases a correct diagnosis is seldom

[1] The antigen used in these tests was kindly supplied by the Division of Zoology, National Institute of Health, Washington, D.C.

made. Finally, it is probable that infestation sometimes occurs without causing any illness in the host. Further investigation of this problem is desirable. Field studies in localities where trichinosis is recognized could provide useful information as to the symptoms and signs of mild trichinosis, and as to the number of persons who do not suffer any illness during an infestation. It is becoming apparent that mild or symptomless cases of trichinosis are far more frequent than are cases in which the so-called typical syndrome is observed. The epidemiology of trichinosis may be comparable with that of poliomyelitis, where manifest illness develops in only a small proportion of individuals exposed to the infective agent.

TRICHINOSIS OF SWINE

The sources of swine trichinosis must be considered in the epidemiology of the human disease, since, with few exceptions, man acquires trichinosis by eating pork. Swine may ingest Trichinæ in the flesh of rats or in scraps of raw pork. The relative importance of these two sources varies in different parts of the world. In the United States, where the incidence of trichinosis in swine is comparatively high, raw pork is the chief source of infection. Swine often have access to this in garbage, due to the fact that garbage-feeding of swine is a common practice in many parts of the United States. Thus the transmission of trichinosis from one generation of pigs to the next is made possible. The lowest incidence of swine trichinosis in America is in areas where grain-feeding is usual, while the highest incidence (sometimes 5%) is in areas where garbage-feeding is the rule. Some persons have contended that garbage-feeding is dangerous not because of pork scraps, but because it attracts rats to the locality, and that swine acquire trichinosis when they eat the rats. This contention is refuted by the fact that boiling of garbage before feeding it to swine, effects a reduction in the incidence of trichinosis, although rats presumably still have access to the garbage, before and after boiling. At present, in America the risk from pork scraps in garbage is so great that, in comparison, swine infection acquired from rats is of little relative importance (Hall, 1937).

The problem of swine trichinosis in Britain appears to be different from that in America. The disease is apparently extremely rare in British swine; actually it has been found in only a few instances. One certain observation was made in Cumberland in 1871 (Dickinson, 1871). Cobbold, confirming that instance, stated: "Hitherto, Trichina has not been observed in our British-fed swine in more than one or two, or possibly three instances" (Cobbold, 1879). In 1927, one thousand carcasses were examined in Birmingham, and no Trichinæ were found, and smaller numbers of animals have been examined on other occasions with negative results (Hardy, 1927). More examinations of this type will be necessary before an estimate of the incidence of trichinosis in British swine can be made. That the condition does occur occasionally is attested by the fact that nearly all of the cases of human trichinosis which have been reported in Britain have followed the eating of locally-produced pork. (This holds true not only for the recent outbreaks, but also for the cases previously reported.)

Principally because of the extreme rarity of trichinosis in British swine the disease can hardly be perpetuated in swine, as in America, by garbage-feeding. A further point which indicates that garbage is not likely to be the source of swine trichinosis in this country is that boiling of garbage before feeding it to swine is required by law. Granting that there may be exceptions to the law, they would not be very dangerous if trichinosis is as rare in British pork as the available evidence indicates.

Trichinosis is endemic in rats in Britain. The condition was noted in Devonshire in 1909 (Harris, 1909). Recent field studies under the direction of Professor R. T. Leiper revealed that rats in Wolverhampton and also in Penrith were infested. Rats probably support the existence of the parasite by cannibalism within their own species, or they may acquire the infection from other animal flesh, as they are scavengers.

The evidence at hand indicates, therefore, that trichinosis is not sufficiently common in British swine to permit the disease to be transmitted continuously within that species, as by garbage-feeding. Trichinosis does exist in rats in Britain, and from this endemic focus an occasional case of swine trichinosis may develop.

EFFECT OF COOKING AND OTHER PROCESSES ON THE PARASITE

The larvæ of *Trichina spiralis* are killed when meat in which they are encysted is cooked sufficiently; a temperature of 60° C. being lethal. This temperature is not always obtained in the central portion of a large roast, after hours in a hot oven (Woodhead, 1895).

Information is lacking in regard to the temperature within a sausage during customary methods of cooking, but the frequent occurrence of trichinosis in persons who have eaten cooked sausage would suggest that a satisfactory temperature is not always obtained. On the other hand the frying of thin slices of ham or bacon should heat all parts of the meat sufficiently to dispose of the parasites. A practical method of ascertaining whether meat has been rendered safe by cooking is to note the colour of the juice which exudes from it. If the juice has become brown or grey, the temperature has been raised to 80° C. Trichina larvæ withstand refrigeration better than cooking. They can live for many weeks in meat kept at 0° C. A temperature of -15° C. will kill them within twenty days. This is a partial safeguard in imported pork. Smoking, salting and drying all have a deleterious action on the parasites, and under proper conditions will kill them (Ostertag, 1934).

HUMAN TRICHINOSIS IN BRITAIN

Although human trichinosis occurs frequently in many European countries and in the United States, it has always been considered a rare disease in Britain. A review of the published reports of cases in the British Isles previous to 1937 lists only twenty-six cases (Van Someren, 1937). Undoubtedly some additional instances were recognized and were not reported in the literature. In the winter of 1940-41 more than two hundred cases of trichinosis are known to have occurred in various parts of England and Wales. These were principally located in Wolverhampton, Birmingham and Penrith, but small numbers of cases occurred in other areas. There has been much speculation as to the cause of this sudden increase in the prevalence of the disease.

A possible explanation of the recent outbreaks of trichinosis in Britain is that an unusually large number of older sows have been slaughtered recently, because it has been difficult to obtain feed for them. Old sows, which are usually used for sausage manufacture, are probably more liable to trichinosis than young pigs, because they have lived longer and have thus had more opportunity to acquire the infection. This is true of man, in whom the incidence of trichinosis increases with age (Hall, 1938).

A peculiarity of the recent epidemics in Britain has been the large proportion of women among persons who were ill. In other countries no such difference between sexes has been noted. The explanation in the present case appears to lie in the fact that women ate raw sausage more frequently than men (Sheldon, 1941).

Another peculiarity of the recent epidemics in Britain is the unusually large number of persons affected in single outbreaks. In Wolverhampton more than one hundred cases were notified; Birmingham and Penrith each had between fifty and one hundred cases. Two conditions may have been responsible: rationing of meat and susceptible population. Rationing of meat increased the number of persons eating sausage. Also, decrease in the proportion of meat in sausages increased the number of persons at risk when a single infested carcass was used in sausage manufacture. There is little reason to doubt that human trichinosis has been rare in most parts of Britain; consequently the general population has had slight opportunity to acquire immunity to the parasite. Such a population would be expected to exhibit a more marked host response to trichinosis than would a population such as that of the United States, which is more or less continuously exposed.

Certain information is desirable in order to assess the extent of the problem of trichinosis in Britain. It would be advantageous to determine the incidence of trichinosis in the human population. Van Someren examined specimens of muscle from two hundred persons in London, and found Trichinæ in only 1% (Van Someren, 1937). Further studies of this type are desirable, as the incidence of human trichinosis may be much higher in other parts of Britain, just as it varies in different parts of the United States. In addition to study of the incidence of trichinosis in human beings, it would be of value to determine the incidence of trichinosis in swine in different parts of Britain. This could be learned from examination of meat obtained in abattoirs. Lastly, examination of rats, cats, dogs and other carnivorous animals would yield information about the distribution of trichinosis in various animal species.

Summary

At the present time only a small proportion of cases of human trichinosis are recognized clinically at the time of their occurrence. The syndrome usually thought to be typical of trichinosis is actually typical only of the severe cases. The majority of persons who suffer infestation have less distinctive illnesses, or have no symptoms whatever. Clinical manifestations of trichinosis depend on the size of the infecting dose and on the resistance

of the individual to invasion by the parasite. Mild or symptomless cases of trichinosis can be detected by means of the differential leucocyte count or by the skin test with Trichina antigen.

Trichinosis exists in rats in Britain. These are probably the sources of occasional cases of infestation among British swine. The available evidence indicates that human trichinosis has been comparatively rare in Britain. The recent increase in prevalence may be due to the use of meat from old sows for sausage manufacture. The large number of persons affected in the recent outbreaks may be attributed either to meat rationing or to the fact that there had been little previous exposure of the population to trichinosis.

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Discussion.—Professor R. T. LEIPER said that with Dr. Beeson he had been associated with the officials of the Ministry of Health in their inquiry into the recent outbreaks at Wolverhampton, Birmingham, Harpenden and Penrith. Aided by a grant from the Agricultural Research Council, a research team, composed of a number of his colleagues at the Institute of Agricultural Parasitology, viz. Dr. Rogers, Dr. Clapham, Miss Young and Mr. J. W. G. Leiper, M.R.C.V.S., had been engaged for some time past on certain parasitological aspects of the problem.

The results of this inquiry, which was still in progress, showed that the outbreaks were attributable to home-bred pigs, that there was no connexion between the outbreaks, that the incidence of trichinosis in the pigs in this country must be low as not a single case had so far been detected microscopically in over 4,000 carcasses, that the rat rather than garbage or swill must be suspected as the source of pig infection here, that routine post-mortems revealed undiagnosed infections in Wolverhampton and Birmingham dating considerably earlier than the recent outbreaks there. Statistics were quoted from official sources to show that although the number of cases of Trichinella detected by the routine State inspection of pigs in Germany was exceedingly low (136 out of 18,153,259 pigs in 1935), nevertheless cases (10 in 1935) of human trichinosis, sometimes fatal, continued to occur there. In this country the occurrence of trichinosis in rats was sporadic but significant. Of rats caught in South London about 25% were infected. At Wolverhampton the only infected rats came from the sewage works, where 2 out of 13 were infected, while at Penrith there was an infection in 9 out of 116 rats caught on the town refuse dump. But of those caught on the farms around Wolverhampton and Penrith so far none had been positive. In spite of careful and detailed inquiry the actual farms from which infected pigs must have come had not been conclusively implicated. At Penrith the suspected source was a small holding some distance from the town and not very remote from the town refuse dump. No infection was found in the pigs remaining there, no rats were obtainable but one of the three cats living on the small holding was found to be infected with *Trichinella*.

From the Penrith rats two pigs had now been experimentally infected and would be used to determine the effects of modern domestic methods of cooking on the viability of the Trichinella cysts. Attention was drawn to the curious prevalence of trichinosis in dogs in the Dutch East Indies although no cases had been detected in man or rats there. Moreover, there was also an equally curious high incidence in the female dogs recalling a similar sex incidence in the Wolverhampton outbreak.

Notes on Preliminary Experiments on the Metabolism of Trichinosed Rats

Mr. W. P. ROGERS, M.Sc., Ph.D., said that the investigation had not covered, as yet, all the lines from which evidence of the effects of Trichinella on the host's metabolism might be obtained and even the figures could not be considered as final.

For the purposes of the preliminary experiments four rats were used. These animals were fed on a standard diet and every four days the urine and fæces from each animal were collected separately. After four periods (each group of four days constituted a period) the animals were infected with *T. spiralis* and the fæces and urine collection continued for a further five periods. It was possible, therefore, to study certain changes occurring in the urine and fæces after infection. Some of these changes found in Rat No. 4 are shown in the table.

SUMMARY OF RESULTS, RAT NO. 4.

Period	Protein digested	Daily N balance	Creatinine per kg. per day	Albumin per day	Ammonia N per day	Remarks
1	81·46%	+ 67·9	19·2 mgm.	25·0 mgm.	7·9 mgm.	No eggs or helminths in fæces.
2	84·27%	+ 62·6	19·7 mgm.	50·0 mgm.	10·5 mgm.	,,
3	80·06%	+ 63·8	18·4 mgm.	60·0 mgm.	7·2 mgm.	,,
4	80·37%	+ 68·8	20·3 mgm.	56·2 mgm.	11·1 mgm.	,,
5	83·02%	+ 47·1	18·9 mgm.	125·6 mgm.	8·4 mgm.	Infected with 680 larvæ. Five larvæ in fæces.
6	79·59%	+ 67·3	20·0 mgm.	125·5 mgm.	6·9 mgm.	Fæces negative.
7	76·94%	+ 54·5	19·7 mgm.	62·5 mgm.	18·4 mgm.	,,
8	81·46%	+ 34·3	23·2 mgm.	70·0 mgm.	13·5 mgm.	,,
9	—	—	34·9 mgm.	75·1 mgm.	7·2 mgm.	,,

No. of *Trichinella spiralis* larvæ found on post-mortem examination, 4,866.

(1) *Protein digestion.*—Digestion was fairly constant except for the fall in the 6th and 7th periods. In all the other rats under examination protein digestion fell during the same periods and in all cases the latter period showed poorest digestion.

The sequence of events occurring in the intestines of the hosts might have been as follows: 5th period, worms too small to cause marked effects; 6th period, the worms grew and the concentration of antiprotease secreted increased; 7th period, the worms not only secreted antiproteases but damaged the intestinal mucosa as they migrated to the lymph spaces; 8th period, the damaged intestinal mucosa was repaired and no more antiprotease was secreted in the intestinal lumen.

(2) *The nitrogen balance.*—This fell irregularly after infection. It seemed probable that toxins secreted by the parasites immediately after infection affected the endogenous nitrogen metabolism, the results being reflected by the amounts of nitrogen in the urine.

Somewhat similar results were obtained from the other animals.

(3) *The creatinine in the urine.*—The figures in the table showed the amounts of creatinine found in mgm. per day per kg. rat weight. There was a marked rise in creatinine during the 8th and 9th periods. This was in some degree due to the fact that there was a fall in the weight of the rat but nevertheless there was a large increase in the absolute amount of creatinine excreted.

Almost exactly similar results were obtained from the other rats under examination except that there seemed to be some relationship between the severity of infestation and the amounts of creatinine excreted.

(4) *The albumin in the urine.*—There was an increase in urinary albumin after infection. Increases were noted in the other animals also but the times at which the increases occurred were not consistent.

(5) *Urinary ammonia nitrogen.*—There was a sudden increase in ammonia nitrogen during the 7th period. Similar results were obtained from the other experimental animals though in one case the rise occurred in the 8th period.

Miss PHYLLIS A. CLAPHAM, D.Sc., said that in the course of an experiment designed to fill in some of the details of the life-history of *Trichinella spiralis*, a rather significant fact emerged—viz. that the nature of the host species played a part in determining the rate at which the female matured and deposited her larvæ.

A group of mice were infected with encysted larvæ and were killed, one each day from the seventh day after infection. Mature gravid larvæ were found in all the intestines and larvæ were obtained from the diaphragm from the tenth day onwards. As no

larvæ were found *en route* for the muscles and as these mice had obviously been killed too soon to show the maturation stages the experiment was repeated, using guinea-pigs as mice were not available. The animals were examined from the fourth day onwards. This time, however, it was soon obvious that while the animals would show the early maturation stages, yet they had been killed too soon to show the migrating stages. For on the seventh day, the females were not even gravid and it was not until the tenth day that larvæ were found free in the intestine, whereas in the mouse they were being liberated on the seventh day. There was a time lag of three or four days.

The course of the maturation in the guinea-pig was as follows: On the fourth day after infection the females had been fertilized but there were no eggs; the following day eggs appeared in the uterus, in the single-celled stage. The next day—sixth—the eggs were seen to be segmenting and on the seventh day they contained larvæ but these were still in the egg shell. On the eighth day they had hatched but were still lying at a considerable distance from the vulva—at about the level of the beginning of the intestine and they remained in this position over the next day—ninth. It was not until the tenth day that the larvæ were found to be filling the whole of the anterior portion of the uterus right up to the vulva. At this time free larvæ were found in the intestine. The animal killed on the eleventh day was unfortunately negative but the last animal killed on the twelfth day contained gravid females and more free larvæ.

The last three animals to be killed were all very lightly infected or negative. These had been fed with meat from the leg, while the others, which contained upwards of 1,000 adults, had been fed with an equivalent amount of meat from the shoulders.

This observation had a practical interest because it showed that the nature of the host species is a factor in determining the time at which muscle invasion begins and hence of the onset of symptoms. At any rate with the human species we must not just blindly calculate back seven days or any other arbitrary number from the first appearance of clinical symptoms and assume that that subtraction represents and coincides with the date of infection.

Clinical Manifestations of Trichinosis in the Pig

Mr. JOHN W. G. LEIPER, M.R.C.V.S., said that little work had been recorded of the clinical picture of trichinosis in the pig, the most important host of this parasite. Maass (*Zentralbl. f. Bakt.*, **129**, 29) in 1933 reported on the eosinophilia developed during the experimental infections of 100, 200, 1,000 and 5,000 encapsulated Trichina larvæ in pigs, and showed that the intensity of the eosinophilia produced was directly related to the intensity of the infection. A maximum eosinophilia was reached between the twentieth and twenty-fourth day after infection, i.e. a period corresponding to the migration of larvæ in large numbers into the muscles. On the forty-second day the white cell count dropped to normal.

In the experiment use was made of four ten-week old pigs; two of these were infected by Dr. R. T. Leiper for the purpose of producing heavily infected trichinosed meat in order to examine the viability of larvæ after curing, cooking, &c.

Pig M1 was given approx. 900,000 viable encysted larvæ from a naturally infected rat.
Pig M2 was given approx. 35,000 larvæ from the same material.
Pigs M3 and M4 were left as controls.

Blood-films from the auricular vein, two days after infection showed 7% eosinophilia, rising gradually to a maximum of 30% on the nineteenth day in the case of pig M1 and to 31% on the seventeenth day in the case of pig M2 and dropping to normal in pig M1 on the twenty-sixth day and in pig M2 on the twenty-ninth day. There was a slight rise again to 10·5% during the next seven days.

Pig. M1 was given a second dose of 43,000 larvæ twenty-nine days after the initial infection, but no noticeable increase in the percentage eosinophilia was demonstrated during the following thirty days. These larvæ were shown to be infective by feeding a rat with the same material which on post-mortem examination was positive, twenty-eight days later. The blood-counts following the second dose suggested that the initial dose had caused the development of resistance in the host.

The clinical picture of the two infected animals was slight, in fact without a comparison with the control animals little that was noticeable resulted from these massive doses. A farmer would probably consider the symptoms due to a slight chill or put it down to the pigs being "bad doers". A week after infection the infected animals were listless, and could be handled more readily than the controls, their appetite was not so good and their progress, from the point of view of growth and increase in weight was quite noticeably behind that of the controls.

From these observations it would seem that diagnosis in the living animal by clinical symptoms and white cell blood counts was not very satisfactory from the point of view of public health. Only if the blood-films were taken during the third week of infection would one suspect the disease: the clinical symptoms alone would be insufficient.

Miss M. YOUNG, B.Sc., said that with a view to finding the farm or particular area from which Trichinella-infected pig or pigs were being supplied to Wolverhampton, Prof. Leiper commenced examining a specimen of diaphragm from every pig killed in the Wolverhampton abattoir. At the same time an order went out that all pigs slaughtered elsewhere were to be brought to the abattoir. There the meat inspectors obtained and labelled a portion of the pillar of the diaphragm of each pig. Later Prof. Leiper asked her to continue the examination of the pork specimens.

To date 4,086 pigs had been examined and all found negative. The first 2,731 specimens were examined both by direct microscopical examination and by the artificial gastric juice digestion method. The remaining 1,355 were examined by the digestion method only, in batches according to their locality, as by that time experience with other infected material showed this to be the most efficient and time-saving method of diagnosis.

Miss Young said further: The first 2,500 specimens of pig diaphragms came from pork pigs, sows and boars. A pork pig does not weigh more than 150 lb., and its life varies from a few months to a year. Compared with the life of sows and boars, usually several to 10 years of age before killing, this short life of pork pigs does not allow long for the possibility of becoming infected with Trichinella. Hence the present pork specimens now being sent for examination from the Wolverhampton abattoir are those from sows and boars only.

In the United States, Hall and Schwartz and others have recorded a 1% incidence of Trichinella in grain-fed pigs and a 4 to 5% incidence in pigs fed on uncooked garbage. In contradistinction to this Mayer, in 1930, published the first positive finding in 100,000 pigs slaughtered and examined in Heidelberg since 1934. There are only two published records of pigs having been examined for Trichinella in this country, viz. by Cobbold in 1870, and by Hardy (and Paul) in 1927. These latter workers found 1,000 Worcestershire pigs to be negative. As it is obvious that a very considerable number of pigs must be examined before a positive result may be expected, the routine examination of boars and sows is being continued.

Whilst the examination of the pork specimens was proceeding in Wolverhampton, the Pathology Department of the Royal Hospital commenced supplying portions of human diaphragms from routine post-mortems, and the second diaphragm examined gave Trichinella cysts with definite though uncalcified cyst walls. The 6th and 7th diaphragms examined also proved positive, and the contrasting conditions of the infections in each case were such as to make quite plain that the infection has been endemic in the Wolverhampton area for many years.

The first three cases of Trichinella infection showed respectively unencysted, encysted though not calcified worms and heavily calcified thick-walled cysts. The unencysted Trichinellæ were from a girl of 23 who had died of endocarditis. The uncalcified cysts were from a woman of 47 who had several months before death been brought to hospital with paralysis of the legs and lower abdomen. She was a housekeeper, also resident in Wolverhampton. The heavily calcified thick-walled cysts were from an elderly man of 63 who was resident in an area just outside Wolverhampton, and whose diagnosis was cardiac infarction. These cysts varied in size and were not all equally calcified, so that he may have been subject to more than one infection through eating infected pork or pork sausages.

In all, so far, 30 human diaphragms have been examined from post-mortem cases in Wolverhampton and of these five were found to be positive, i.e. approximately a 17% incidence. The fourth positive case was a woman of 46 who had died after an operation for partial gastrectomy. The Trichinella worms were unencysted and were identical in appearance with those found in the girl of 23. It is therefore suggested that the infection was acquired at the same time, possibly from the same batch of infected pork or sausage-meat. The fifth positive case was a man of 45 resident in an area near Wolverhampton, the diagnosis given being coronary occlusion. The cysts found were all extremely heavily calcified and the worms were hardly distinguishable as such in the centre of the cysts. In contradistinction to the other heavily calcified case, the cysts were almost identical in size and amount of calcification.

From these results in Wolverhampton it was thought of interest to examine diaphragms from post mortem cases in other areas of England, and a small number have already been dealt with.

The results are as follows:

HUMAN DIAPHRAGMS EXAMINED FOR "TRICHINOSIS".

Locality	No. examined	No. positive
Wolverhampton	30	5
Birmingham	5	1
Cambridge	2	0
Bristol	5	0
Cardiff	3	0
Llandough	2	0
Total	47	6

The one positive case so far obtained from the small number examined from Birmingham confirms the endemic character of Trichinella infection in the Midland area. This infection was found to be the heaviest yet obtained and cysts were seen in the direct microscopic examination of muscle pressed between two slides, as well as in very large numbers in the digest sediment. They were thick-walled and showed polar calcification. The man was only 36 years of age, a resident in Oldbury, and the diagnosis given was cerebral embolism and subacute infectious endocarditis.

It may be of interest to note that of the six positive cases the diagnosis given of four was of a cardiac nature.

The incidence of Trichinella infection in 30 post-mortems at Wolverhampton was at first sight puzzling, for all 5 positives were found in the first 15 specimens. On looking carefully at the data supplied it appeared that these positives were 3 out of 10 women, i.e. 30% incidence, and 2 out of 20 men, i.e. 10% incidence. This confirms the findings in the January epidemic by Dr. Sheldon who found a four to one female preponderance, and traced this to the not infrequent habit, particularly prevalent among women, of eating raw sausage meat either while cooking it or as sandwich spread.

None of the six infections obtained so far was diagnosed during the life of the patients.

Diaphragms for testing will be gratefully received if posted to the Institute of Agricultural Parasitology, Winches Farm, St. Albans, Herts.

REFERENCES

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HARDY, T. L. (1927), *Lancet* (ii), 1380.

Dr. R. H. H. JOLLY (*Medical Officer of Health, Wolverhampton*), made the following observations on trichinosis:

(1) *Onset.*—The outbreak of trichinosis in Wolverhampton and district included 130 clinical cases of the disease, 98 being in the town itself and 32 in surrounding districts. The onset of symptoms (i.e. œdema of the face), in the first case was on December 12, 1940, and in the last case on March 5, 1941. Full reports were obtained on 124 cases.

(2) *Age and sex distribution.*—Adult males 13 cases; single females 19 cases; married females 69 cases; children 23 cases.

An inquiry from 767 working-class families in different parts of the town gave the following results:

280 families, or 37%, admitted the habit of eating raw sausage. In 174 of the above, or 23%, the habit was confined to the housewife. In 106, or 14%, raw sausage was eaten by the members generally.

(3) *Source.*—Several firms of sausage manufacturers were involved in the inquiries, but 60% of the cases were definitely traced to three separate manufacturers A, B and C.

A—12 cases; B—26 cases; C—37 cases. Total 75.

The same three firms were purveying 60% of all the sausages consumed in Wolverhampton and district (i.e. 16,000 lb. out of a total of 26,900 lb. per week).

(4) *Incubation period.*—In spite of the detailed investigations carried out by Prof. Leiper and his staff no infected swine were discovered nor have any infected rats been detected from the farms in Staffordshire and Shropshire from which the manufacturers obtained the major part of their supplies. This suggests that a minimal number of trichinosed swine must have caused the outbreaks attributable to these three manufacturers. It is not improbable that one infected animal may have been the cause of all the cases traced to firm (C), and similarly one animal may have given rise to all the cases attributable to firm (A). If this assumption is made the incubation period must have varied from eight to fifty days because the cases attributable to firm (A) were spread over a period of four weeks and those to firm (C) were spread over a period of six weeks.

In five of the six severe (i.e. hospital) cases which were definitely traced to one of these three firms, the onset of symptoms was at the beginning of the epidemic and these cases were among the first to be reported. (1) Does the length of incubation depend upon the severity of the infection, and (2) can the incubation time be lengthened if the patient has previously suffered from a mild subclinical attack of trichinosis producing a partial immunity?

(5) *Endemicity.*—Miss Young's investigations with post-mortem human specimens have definitely demonstrated that trichinosis is endemic in the Black Country. Van Someren's review of previous outbreaks of the disease in England and Wales suggests that the same may be true about other parts of the country:

Wolverhampton: 1 case in 1850. Outbreak in 1941.
Cumberland: 3 cases Workington 1871. Outbreak Penrith 1941.
Milford Haven: 1 case in 1922. 3 outbreaks in South Wales in 1939 and 1940.
Smethwick: 2 cases in 1927. Outbreak in Birmingham 1941.

Section of Medicine

President—Sir Maurice Cassidy, K.C.V.O., M.D.

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Mass Radiography in the Early Detection of Intrathoracic Disease

(With Special Reference to Pulmonary Tuberculosis in Recruits)

By Philip Ellman, M.D.

The detection by radiology of definite pulmonary disease, despite the absence of physical signs, is now becoming increasingly recognized, and all competent authorities are familiar with the "silent lesion" in a widespread disease like pulmonary tuberculosis.

I propose in this paper to deal principally with the subject as it affects the early diagnosis in war of minimal pulmonary tuberculosis in presumably healthy recruits to the services, to war industry, &c., not omitting certain non-tuberculous pulmonary diseases and cardiovascular diseases detected in the course of such routine mass examinations. In relation to cardiovascular disease W. A. Jones (1940) in a survey of the results of routine chest X-ray examinations of Canadian recruits states that "while the contribution of radiology to the early diagnosis of silent clinical pulmonary lesions is generally accepted and is so well known as not to require discussion, it is not so generally accepted that X-ray methods of measuring the size of the heart are immensely more valuable than clinical methods and that, in fact, percussion is no longer considered an accurate method of cardiac measurement". Jones states that as a result of his survey this view is amply confirmed by the number of enlarged hearts discovered by X-rays after they had been passed by medical boards as normal in size.

Pulmonary tuberculosis is, however, the most important chronic infectious disease affected by war, and in spite of all recent advances it is still responsible for the highest death-rate in young adult life. The influences of under-nourishment associated with the food problem, overwork, prolonged physical or mental stress and strain, are responsible for the infected becoming the clinically tuberculous. During the Great War of 1914-18 statistics show that some 25,000 more deaths, mainly confined to young people occurred than would have done, had the 1913 death-rate continued, and, according to the Annual Report of the Chief Medical Officer of the Ministry of Health (1920), the greater industrial employment of women was in part responsible for this increase. From the figures so far obtained and from one's own general impression gained in clinical practice there is evidence that the death-rate is already increasing in the present war.

In young adolescents in particular early pulmonary infiltration may be completely asymptomatic; in a large proportion of cases physical signs may be entirely absent. In this age group more particularly, even extensive lung changes may be accompanied by few clinical manifestations. The great obstacle in the past to the early discovery of pulmonary disease has been the fact that patients have rarely visited their doctor until confronted with symptoms, by which time some 75% of cases are moderately advanced.

Under present conditions patients are only referred to Out-patient chest clinics when symptoms are manifest and not more than 5% of cases are detected while the lesion is minimal.

It follows, therefore, that improvement in early diagnosis, a vital necessity despite all recent advances, with a corresponding improvement in the recovery rate, must depend upon the recognition of the disease before it has produced symptoms of impaired health. In future diagnosis must accordingly be considered in two groups of the population (*a*) the symptomatic subject referred to the physician (in the past he has been our principal concern), (*b*) the apparently healthy asymptomatic subject whom the physician must go out to seek. As Sir James Mackenzie (1919) in the "Future of Medicine" has stated: of the four stages of disease we must concentrate on Stage I, the preclinical asymptomatic stage.

Just as chest radiology can contribute to modern knowledge of many diseases of the heart and lungs, mass chest radiography may in the future have an even greater part to play, particularly in the sphere of preventive medicine. Periodic health examinations, already familiar in America, will demand the close association of the agencies for preventive and therapeutic medicine, hitherto poles apart, and possibly the medicine of the future, which will require also to be more intimately connected with social and economic conditions, will have as its main object the maintenance of health rather than the cure and palliation of disease.

Case-finding programmes will need to be instituted, the purpose of which will be to detect as rapidly and as economically as possible significant intrathoracic lesions. It has been the experience of many observers in Europe, Australia, America and Canada and more recently in this country that mass X-ray examination of the chest offers the best-known single means of detecting shadows of such lesions in presumably healthy people and by this method, according to the population group selected, from 0·5% to as much as 5% have been found to have minimal lesions. It must of course be recognized that they are macroscopic and, when they are detected, the finer diagnostic procedures will be needed to determine their exact ætiology and clinical significance, for, although the tubercle bacillus is the commonest cause of such pulmonary lesions, other diseases of a non-tuberculous nature may cast radiological shadows closely simulating pulmonary tuberculosis (Davidson and Ellman, 1941).

The methods available for mass radiography are:

(1) *The full-sized chest radiograph.*—This is probably ideal but, apart from being a lengthy procedure it is far too expensive for mass examinations. This, in itself, has been a reason for the limitation of radiological surveys in the past. I was, however, able to make an examination of this type in a contact service from which the following noteworthy figures were obtained: Of 2,681 presumably healthy subjects, known to have been in contact with cases of, for the most part, open pulmonary tuberculosis, 257 (i.e. 9·6%) were discovered to have lesions and of these 181 were significant and required treatment (i.e. 6·75% of the total number of cases examined). It is of interest to note that in at least 65% of the abnormal cases clinical examination alone would have failed to detect any lesion. It must, however, be remembered that in a selected group of contacts this examination is likely to be particularly fruitful from the point of view of results. A further point of interest arising from these figures is that abnormalities in the cardiac silhouette were primarily responsible for the detection of five cases of mitral stenosis, two of aortic incompetence of rheumatic origin, eight of hypertensive heart disease, and two of specific aortitis, all of these in symptomless persons. In other words, in the course of a mass X-ray survey, in addition to the pulmonary lesions mentioned, 17 cases of cardiovascular disease were discovered (i.e. 0·63%).

(2) *Sensitized paper instead of an X-ray film.*—This is a less expensive method, although the cost is still relatively high, and interpretation is not, even at the best, very reliable.

(3) *Fluoroscopy or screening.*—With an experienced observer this method is an inexpensive and accurate means of detecting macroscopic lung lesions and certain cardiac lesions. Indifferent results can frequently be ascribed to failure to wait for dark adaptation. Fellows and Ordway (1937) in a study to estimate the accuracy of this method as opposed to physical findings in the mass examinations of policy holders of the Metropolitan Life Insurance Company of America compared their results with full-sized film controls and found that in 2,603 examinations 87% of pulmonary lesions were detected by fluoroscopy. Assuming, as they had, that the direct film reveals 100% of lesions of pulmonary tuberculosis their results were:

Revealed by X-ray	100%
Revealed by fluoroscopy	87%
Revealed by physical examination	36%
Revealed by symptoms	33%

In the medical division of this company some 25,000 physical examinations, supplemented by fluoroscopic chest examinations are made annually.

In an analogous investigation of 3,229 screen examinations which I have made during the last few years with control films to try to determine the accuracy of the method I found that in 94% of cases the interpretation of the screen findings coincided with the interpretations of the films. While therefore the method is not infallible, it is rapid and economical for mass examinations. On the other hand the physical risk to the examiner and the absence of a permanent record are pronounced disadvantages.

(4) *Miniature screen photography* is in my view the most practical, reliable and economic single means of detecting intrathoracic lesions in large groups of presumably healthy individuals. It has been used extensively in several countries and has excited great interest in this country since the war owing to its possible application to the examination of recruits to the Services and, as I believe, of female adolescent recruits to war industry. Its possible extension in peacetime to the periodic health examinations of adolescent industrial workers, to those engaged in certain trades where the pneumokonioses are common, and to groups of the population where pulmonary tuberculosis is high, especially in a contact service, opens a new and extensive problem in the domain of public health. Certain results of such surveys of the ordinary population are already available and it cannot be doubted that the method more boldly applied, ensuring as it does more accurate diagnosis, will effect a considerable saving to the State in the cost of treatment and pensions where a disease has been wrongly diagnosed, a not infrequent occurrence in the exigencies of war and rapid recruiting, when a purely physical examination may be made without ancillary aids. Since the Great War, there are cases still receiving pensions for presumed lung tuberculosis which is in fact, non-existent. On the other hand some of us are seeing cases of pulmonary tuberculosis, passed in this war by recruiting boards, who had lesions before they joined the Forces.

TABLE I.—PERCENTAGE OF CASES OF ACTIVE PULMONARY TUBERCULOSIS FOUND BY MASS X-RAY EXAMINATION OF PRESUMABLY HEALTHY GROUPS.

AUSTRALIA.			
Australian Army.	Galbraith, 1941 (in 100,000 recruits)	0·56%	
Australian Army.	Cooper, 1940 (in 9,000 recruits)	0·55%	
CANADA.			
Canadian Army.	Jones, 1940 (up to April, 1940)	1% approx.	
GREAT BRITAIN.			
Royal Navy.	Dudley and Fitzpatrick, 1941 (47 active cases in 18,000 examinations)	0·26%	
	Hart, Hilton and Morland (student service, 417)	5%	
	Wingfield and McPherson (group of 2,000 secondary school-boys and adolescent industrial workers)	*Definite* 0·65%	*Possible* 1·08%
	Ellman (among 601 presumably healthy recruits).. ..	0·83%	
	Ellman. Contact service (2,681)	6·75%	9·6%
U.S.A.			
	Hetherington and McPhedran (student service)	3·9%	
	Stiehm (student service)	1·5%	
	Soper and Wilson (student service)	1·8%	
GERMANY			
	Kattentidt (students)	2·0%	
	Berner (over 55,000 recruits, Army and industry) ..	1·5%	
SPAIN.			
	Sayé (students)	4·5%	
CHINA.			
	Hall and Chang (young adults)	17·9%	

This method of mass radiology has been adopted in the selection of volunteers for the Australian Expeditionary Force and has been extended to the permanent military forces

and garrison battalions (Cooper, 1940, in an examination of 9,000 recruits found active pulmonary tuberculosis in 0·55%). Galbraith (1941) in a valuable communication reports a further extension of this work and the results of 100,000 examinations by this method. 1 in every 100 showed X-ray evidence of active and latent lesions, 1 in 200 of active tuberculosis, 1 in 400 of non-tuberculous lesions and 1 in 1,000 had cardiovascular abnormalities. In this country the results of the pioneer work of the medical personnel of the British Navy, recorded in a report on the examination of 18,000 subjects (Dudley and Fitzpatrick, 1941) show that among 7,000 trained men and the remainder new entrants there were 47 active cases of pulmonary tuberculosis (i.e. 0·26%) (Table I).

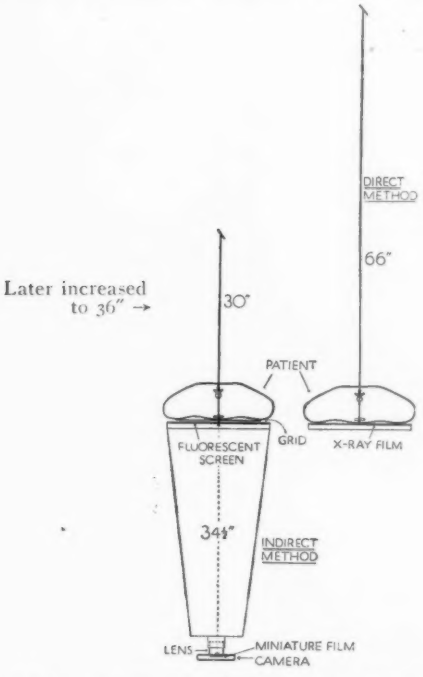

FIG. 1.—Plan diagram showing relationship of tube, patient, screen and camera for taking a miniature radiograph and relationship of tube, patient and film for taking a direct radiograph. (By courtesy of the *British Journal of Radiology*.)

Technique of the method.—This has been detailed in a previous article by Clark, Cordiner and myself (1941).

The present technique of miniature screen photography has been gradually developed since 1896 when Bleyer in this country discovered a means of registering the fluorescent screen image on a photographic plate. It was not, however, until 1936 that de Abreu of Rio de Janeiro first recorded this application of the method to mass examinations, and its practical and routine applications have been made possible by the tremendous improvement of recent years in fluorescent screen and lens construction and in photographic material. For miniature screen photography the activated fluorescent screen image is photographed on a small 35 mm. film and the camera used is one such as a Contax or Leica with a lens having an aperture of F.1·5 and 2 in. focal length. In the study which we made, for the technical aspects of which Miss Clark of the technical and radiographic dept. of Messrs. Ilford Ltd., and her staff were responsible, the Contax camera was placed at one end of a light-proof tunnel, at the other end of which was a Levy-West ordinary yellow green

fluorescent screen. A stationary grid was attached to the tube side and the whole was mounted on a stand which allowed of vertical movement. During operation the unit was placed in front of the X-ray screen, the camera to screen distance being 34½ in., the tube to screen distance 30 in. later increased to 36 in., and the exposure time varied from 0·2 to 0·4 of a second. For rapid exposure of 200 cases per hour it is important to have:

(*a*) Linked control of X-ray exposure, camera shutter and movement of the film in the camera.
(*b*) Automatic adjustment of tube and film to height of patient.
(*c*) Simple and adequate means of identifying the patient with his own film.
(*d*) A camera fitted to take a large roll of film.

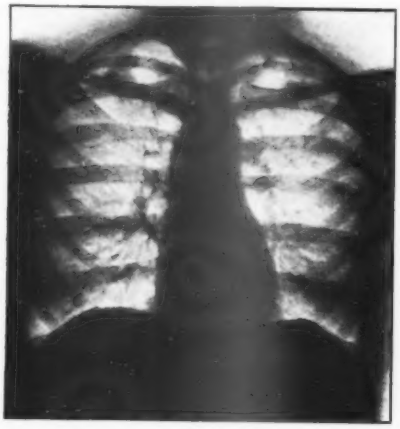

FIG. 2A.—Enlargement from a miniature radiograph.

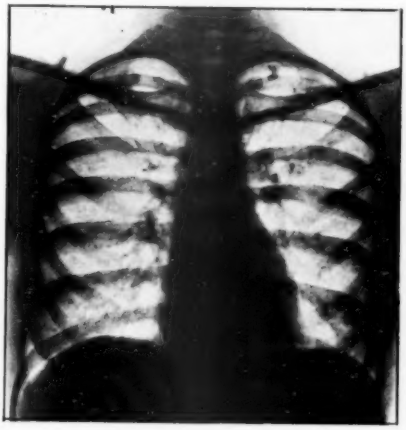

FIG. 2B.—Reduction from a 15 in. × 12 in. direct radiograph.

FIG. 3A.—Enlargement from a miniature radiograph.

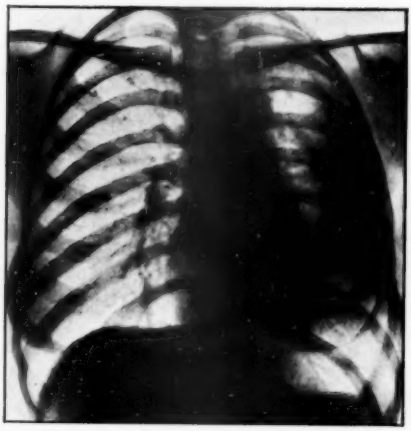

FIG. 3B.—Reduction from a 15 in. × 12 in. direct radiograph.

The actual exposure technique has also been detailed in a previous paper. The miniatures can be projected to almost full-size but 10 in. × 8 in. or 12 in. × 9 in. is the size of choice for reporting on them. This involves work in a dark room and the process of viewing and reporting can prove a tiring process. It is, however, possible to examine up to 200 films per hour. I agree with Dr. Shanks (1941) and others that the films should, for preference, be viewed by a team of two, i.e. physician and radiologist, and that for recruits to the Forces a miniature photograph should in the future be part of the medical board examination. Ultimately, this diagnostic aid will be considered as necessary and as important in a general overhaul as routine examination of urine, blood-pressure, &c.

In order to assess the practical value of miniature screen photography, Clark, Cordiner and I, working as a team of technician, radiologist and physician, have co-operated in an experimental study with direct radiographs as controls. We recognized at the outset and emphasized in a previous paper that it is no less important for the miniature film to be technically satisfactory than the full-sized direct radiograph, since without such technical exactitude correct interpretation is not only impossible but is fraught with danger and would have a prejudicial effect on what we believe to be a valuable method for mass X-ray surveys.

We have therefore collaborated with a view to deciding on the most suitable type of negative to meet the requirement of correct interpretation. The initial work, undertaken by Miss Clark, involved the examination of more than 300 subjects and was followed by the examination of 60 patients attending my out-patient chest clinic. The films of these 60 patients, together with 20 presumably healthy subjects (miniature and full-sized radiographs) have been interpreted by Dr. Cordiner and myself independently. Our results have already been recorded. Our interpretations of the indirect and direct films were practically identical in all but 8 cases. In 1 case the direct radiograph revealed a lesion unsuspected in the miniature (a small apical pneumothorax). In 4 cases the full-sized radiograph disproved the presence of lesions suspected in the miniature two of which, although suspicious, were regarded then as probably normal. Of the 3 remaining cases an Assmann focus suspected on the miniature was confirmed by the direct film, a suspected active lesion in the miniature was disproved by the direct film, and the exact nature of a suspected basal lesion was revealed by the direct film.

Subsequently, through the courtesy of Miss Clark, Dr. Poulsson of the Norwegian Medical Service and Dr. Courtney Gage, I investigated by this method, again with direct radiograph controls, 601 cases of Norwegian recruits, mainly from the Lofoten Islands. I was able to see the miniature and direct films of almost all the cases and record my interpretation of them. My findings were then compared with the independent interpretation of two radiologists, Dr. Courtney Gage, Director of the Radiological Department, St. Mary's Hospital, and Dr. Poulsson (Clark and Poulsson, 1941, have just recorded a detailed and more extensive series of cases).

Results of analysis.—The films of 601 recruits were examined. Of these 550 were unquestionably normal and my interpretations coincided exactly with those of Dr. Gage and Dr. Poulsson. 29 lesions were suspected in the miniature (4·83%) and con-

TABLE II.—RESULTS OF AN ANALYSIS OF THE EXAMINATION OF 601 RECRUITS BY MINIATURE SCREEN PHOTOGRAPHY WITH DIRECT RADIOGRAPH CONTROLS.

550 were unquestionably normal. 29 lesions (4·83%) were detected.

No. of recruits showing X-ray evidence of active pulmonary tuberculosis (including 2 pleural effusions)	5 (0·83%)
No. of recruits showing X-ray evidence of calcified healed lesions	8 (1·3%)
No. of recruits showing X-ray evidence of fibrotic pulmonary lesions (healed or quiescent)	4 (0·65%)
No. of recruits showing X-ray evidence of non-tuberculous pulmonary lesions	6 (1%)
No. of recruits showing X-ray evidence of cardiovascular lesions	3 (0·5%)
(Hypertensive type of heart	2)
(Aortitis	1)
(Prominent pulmonary conus, of doubtful significance (not included)	2)

firmed by the direct radiographs and in 4 of these our interpretations varied somewhat. 22 miniature films which were not free from suspicion were disproved by the direct films.

The practicability of the method has, I think, been demonstrated by the experience of Cooper, Galbraith, Dudley, and Fitzpatrick and ourselves as well as by that of workers in other countries.

TABLE III.—PERCENTAGE OF CASES OF CARDIOVASCULAR LESIONS FOUND BY MASS X-RAY EXAMINATIONS OF PRESUMABLY HEALTHY GROUPS.

Australian army recruits (100,000), (Galbraith, 1941)	..	0·12%
Recruits to Canadian Services up to April, 1940 (Jones, 1940)	..	0·294%
German militia and industrial workers (55,666) (Berner, 1939)	cardiac	2·27%
	aortic	0·56%
Recruits to Norwegian Service (601) (Ellman, 1941)	.. ..	0·5%
Examinations of contact service of 2,681 (Ellman, 1941)	..	0·64%

The limitations of the method are obvious but the main purpose of the miniature film is to serve as a diagnostic sifter and not as a substitute for direct X-ray films or for clinical, bacteriological, or other investigations. As Cooper rightly emphasizes, enthusiasm for a relatively cheap method of detecting pulmonary lesions must not be allowed to outstrip caution and thus do harm to a valuable advance in preventive medicine and particularly in the control of pulmonary tuberculosis.

SUMMARY

Some results are recorded by (1) full-sized radiographs, (2) fluoroscopy, (3) miniature screen photography. The most practical means of carrying out mass X-ray examinations of the chest is by miniature screen photography.

From personal experience of an investigation of this method with control experiments I would say:

(1) For correct interpretation miniature screen photography demands a technically satisfactory film which involves the co-operation of technician, radiologist and chest physician.

(2) Miniature screen photography makes an invaluable contribution to the detection of preclinical asymptomatic pulmonary lesions in the presumably healthy population. It can, therefore, add much to the prevention and control of pulmonary tuberculosis in war by the examination of recruits to the Services and in peace by the examination of selected groups of the population, such as adolescents in industry, where pulmonary tuberculosis rate is high and in certain trades where pneumokonioses are common.

(3) The method has its limitations (as has also the full-sized direct radiograph). Lesions detected are macroscopic and their discovery by this method must not preclude the use of the finer diagnostic procedures.

(4) The extension of the method to the sphere of cardiology in the detection of asymptomatic, preclinical, cardiovascular lesions among such examinations is noted.

(5) Serial examinations by this method as a preventive measure is advocated and its general adoption in routine health examinations is urged.

Students should be trained to concentrate not, as in the past, purely on established disease but also on the preclinical case with a view to preventing disease. This is best done by co-ordinating preventive and therapeutic medicine.

[For the purposes of comparison a series of films were shown of the miniature radiographs enlarged to 10 in. × 8 in. together with the corresponding full-sized direct radiographs.]

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The following participated in the subsequent discussion: Dr. J. B. Sparks, Dr. M. Davidson, and Dr. G. Marshall.

Galactose Tolerance in Jaundice and Hyperthyroidism

By N. F. MACLAGAN, M.Sc., M.D., M.R.C.P.

THE galactose tolerance test has been widely used to test liver function since its introduction by Bauer in 1906, and very divergent opinions have been expressed as to its clinical value. I shall give some results obtained with a recent modification of the test in which the blood galactose is estimated after the oral administration of 40 grm. of the sugar. This method depends upon the use of yeast to remove blood glucose. The alternative methods which depend upon the estimation of either urinary galactose or total blood-sugar both have certain disadvantages, and it appeared that the test in this new form was worth a further trial in jaundice, in view of the encouraging preliminary results already published.

If liver function tests are required in cases of jaundice, it is usual to distinguish toxic from obstructive jaundice. This may be difficult both clinically and pathologically, so that we even find a classification of jaundice proposed by Rich (1930) where no distinction is recognized between the two, which are classed together as regurgitation jaundice. But even admitting the difficulty of demonstrating any consistent differences in the bile pigments in the two conditions, either by the van den Bergh reaction or by any other procedure, the more usual classification of McNee (1922) is still to be preferred because it is so often of vital importance to know whether the jaundice is the result of mechanical obstruction which can be removed, or of hepatic necrosis which cannot. The best method would appear to lie not in a refusal to distinguish the two types, but in studying a function of the liver unconnected with the excretion of bile, such as the glycogenic function. We might reasonably anticipate a greater disturbance of the glycogenic function in the toxic than in the obstructive type.

In this series of 48 cases of jaundice the diagnoses given are those arrived at on clinical grounds by members of the honorary staff of Westminster Hospital and of King Edward VII Hospital, Windsor, to whom my thanks are due for permission to investigate their patients. In the obstructive group, the details are fairly complete, being based on operative findings in 18 out of the 24 cases. The toxic group are necessarily not quite so well established, but a full clinical examination had always been undertaken, including cholecystography in many cases. Moreover, complete recovery occurred with medical treatment in most of those cases labelled common infective jaundice. Cases in which the diagnosis was at all doubtful have been omitted. With reference to the controversy over the existence of two types of common infective jaundice ("catarrhal jaundice") as suggested by Hurst and Simpson (1934) and disputed by Cullinan (1939) I may point out that all the 17 cases of this condition showed impairment of glycogenic function

which suggests that none of them was of the obstructive type, but that the jaundice was due to a mild hepatic necrosis. It is true that one of these cases gave the flat type of curve which appears to be characteristic of biliary obstruction. This curve was, however, from a man of 71 jaundiced for only five days, and none of the obstructive cases with a history as short as this showed any impairment of tolerance. I hope that this obstructive type of common infective jaundice will prove to be as rare as these figures suggest, because it would obviously be impossible to distinguish it from obstruction due to other causes by any liver function test.

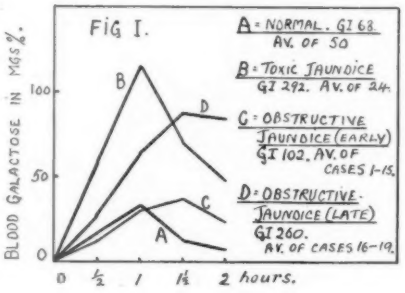


FIG I.
A = NORMAL. GI 68. AV. OF 50
B = TOXIC JAUNDICE GI 292. AV. OF 24.
C = OBSTRUCTIVE JAUNDICE (EARLY) GI 102. AV. OF CASES 1-15.
D = OBSTRUCTIVE JAUNDICE (LATE) GI 260. AV. OF CASES 16-19.
BLOOD GALACTOSE IN MGS %.
100
50
0
B
D
C
A
0 ½ 1 1½ 2 hours.

The technique of the test and the results obtained with 50 normal persons are described elsewhere (Maclagan, 1940). Fig. 1 shows first of all an average normal curve (Curve A). The principal points to notice about this are that the highest value in normal subjects usually occurs at one hour and does not exceed 80 mgm.%. The sum of the four half-hourly values for which the name galactose index has been suggested, should not exceed 160, and averages 68. The other two curves show the average results in jaundice. It will be noted that the curve in toxic jaundice shows frank hepatic impairment with a peak shape curve (Curve B). The results with the 24 cases of obstructive jaundice may be divided into three groups. 15 cases gave results within normal limits with curves which were usually abnormally flat in shape (Curve C). 4 cases showed moderate impairment of tolerance (galactose index between 160 - 300) but with very flat curves (Curves D). 5 cases showed varying degrees of impairment with peak shape curves which would be indistinguishable from those seen in toxic jaundice.

Considering now the curves individually, it is found that 22 out of the 24 cases of toxic jaundice correspond to the average curve with galactose indices varying from 178 - 584 (Table I). The remaining 2 cases gave high indices, 191 and 287 respectively, but with flat curves (underlined in Table I). One of these was a case of atophan poisoning and the other the single case of common infective jaundice already referred to. As a criterion of flatness the difference between the highest reading and the two-hour reading has been calculated, and the curves have been classified as flat if this value is less than 20. For comparison, this figure averages 41 in normal subjects, and 68 in cases of toxic jaundice. In obstructive jaundice the three groups already mentioned are indicated in Table II. This table does not look exactly promising at first sight, but becomes more so when we take into account the length of the history. Most of the patients or their doctors were questioned by me personally on this point, and the greatest effort was made to get a reliable figure of the exact duration of jaundice up to the time of doing the test. It will be seen that all the obstructive cases showing impairment had a history of at least four weeks' jaundice, or had had recurrent attacks of jaundice. The 15 cases with normal function had histories of from four days to eight weeks.

The distribution of cases is further illustrated in Table III, from which it appears that the test should be helpful in distinguishing toxic from obstructive jaundice if used with discretion. While admitting that a larger series is desirable, the following conclusions appear to be justified: A normal curve indicates an obstructive type of jaundice, and a

TABLE I.—TOXIC JAUNDICE.

No.	Diagnosis	Age and sex	Gal. index	Shape of curve*	Duration of jaundice	Serum bilirubin mgm.%
1	N.A.B. therapy	28 M.	178	Peak (87)	3½ weeks	—
2	Com. inf. jaundice	21 M.	183	,, (94)	2 days	5·3
3	,, ,, ,, ...	71 M.	191	Flat (0)	5 days	4·0
4	Hepatic cirrhosis	56 F.	199	Peak (81)	Chronic	—
5	Comm. inf. jaundice	51 M.	204	,, (64)	7 days	3·5
6	Gold therapy	31 M.	213	,, (74)	—	2·4
7	Comm. inf. jaundice	38 F.	220	,, (45)	10 days	4·1
8	,, ,, ,, ...	20 M.	231	,, (103)	5 days	2·4
9	,, ,, ,, ...	20 M.	231	,, (86)	4 weeks	—
10	,, ,, ,, ...	36 M.	247	,, (35)	5 days	4·9
11	,, ,, ,, ...	50 F.	248	,, (63)	4 weeks	10·7
12	,, ,, ,, ...	27 M.	249	,, (146)	2 weeks	5·6
13	,, ,, ,, ...	43 M.	256	,, (93)	3 weeks	9·4
14	Hepatic cirrhosis	47 M.	262	,, (65)	Chronic	3·0
15	Comm. inf. jaundice	66 F.	268	,, (47)	—	2·2
16	,, ,, ,, ...	62 F.	273	,, (97)	5 months	2·4
17	Atophan therapy	50 F.	287	Flat (10)	Chronic	12·2
18	Comm. inf. jaundice	59 M.	367	Peak (95)	4 weeks	11·6
19	Sulphanilamide therapy ..	25 F.	341	,, (60)	1 week	—
20	Comm. inf. jaundice	33 F.	382	,, (66)	6 days	11·1
21	,, ,, ,, ...	46 F.	428	,, (55)	4 weeks	—
22	,, ,, ,, ...	45 M.	470	,, (39)	Some weeks	—
23	Industrial hepatitis	19 F.	497	,, (73)	Recurrent	4·0
24	Hepatic cirrhosis	54 F.	584	,, (53)	Chronic	5·3

* The figure in brackets is the difference between the highest blood galactose and the two-hour value, in mgm. %.

TABLE II.—OBSTRUCTIVE JAUNDICE.

No.	Diagnosis	Age and sex	Gal. index	Shape of curve*	Duration of jaundice	Serum bilirubin mgm.%
1	Pancreatitis	54 F.	31	Flat (0)	17 days	7·2
2	Gall-stones	66 F.	53	,, (0)	4 days	—
3	Carc. panc.	45 F.	59	,, (0)	8 weeks	17·0
4	,, ,, ...	62 M.	71	Peak (26)	4 days	9·1
5	,, ,, ...	73 F.	81	Flat (2)	14 days	13·1
6	Gall-stones	58 F.	83	,, (17)	23 days	8·1
7	Glands in portal fissure ..	58 M.	101	,, (10)	6 days	10·9
8	Carc. panc.	58 F.	108	Peak (31)	6 weeks	14·8
9	,, ,, ...	54 M.	113	Flat (3)	8 weeks	—
10	,, ,, ...	59 F.	120	Peak (22)	2½ weeks	14·1
11	,, ,, ...	71 M.	129	Flat (0)	—	15·7
12	Glands in portal fissure ..	34 F.	130	,, (16)	5 weeks	13·2
13	Gall-stones	50 F.	144	Peak (30)	Recurrent	6·8
14	Carc. gall-bladder	55 F.	146	,, (39)	14 days	4·9
15	Glands in portal fissure ..	73 M.	160	Flat (5)	3 weeks	20·9
16	Carc. panc.	68 F.	209	,, (1)	Recurrent	9·4
17	,, ,, ...	75 F.	248	,, (1)	7 weeks	13·5
18	Carc. gall-bladder	56 F.	279	,, (0)	4 weeks	16·2
19	Gall-stones	69 F.	305	,, (10)	Recurrent	—
20	Carc. panc.	62 F.	249	Peak (39)	9 weeks	17·9
21	Gall-stones	38 F.	309	,, (27)	4 weeks	10·0
22	Carc. panc.	67 F.	258	,, (25)	10 weeks	16·0
23	Carc. gall-bladder	66 F.	387	,, (49)	7 weeks	—
24	Carc. gall-bladder	65 F.	443	,, (57)	4 weeks+	11·4

* The figure in brackets is the difference between the highest blood galactose, and the two-hour value, in mgm. %.

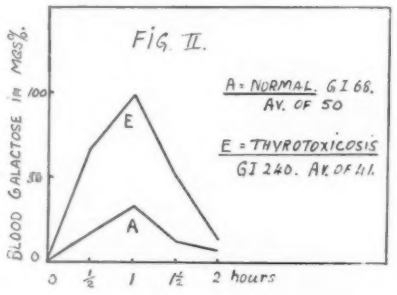
TABLE III.

Galactose tolerance (Gal. index)	Obstructive jaundice Duration of jaundice	No. of cases	Toxic jaundice No. of cases
Normal (0—160) ..	.. 4 days to 8 weeks	15	0
Moderately impaired, flat curve (160—300)	All at least 4 weeks or recurrent attacks	4	2
Impaired, peak curve (over 160)		5	22

moderately high flat curve is also suggestive of obstruction. A high peak-shaped curve indicates either toxic jaundice or biliary obstruction which has lasted for a considerable period. Looked at from another angle, there should be a good prospect of distinguishing the two types if the case is seen within the first two or three weeks of jaundice, and after this there is still some hope of doing so but only if a normal or moderately high flat curve is encountered. A high peak curve after three weeks may indicate either variety. In this connexion, a history of recurrent attacks of jaundice must be taken as possessing a similar significance to a long history.

As to absorption from the alimentary tract, the test must of necessity give misleading results if there is pyloric stenosis or nausea and vomiting from any cause; this has sometimes meant postponing the test for a few days, particularly in cases of common infective jaundice with much gastro-intestinal disturbance.

Some such relationship to the length of history was to be anticipated in view of the well-known effects of prolonged biliary obstruction on the liver. Gibson and Robertson (1939) make a distinction between continuous obstruction which is said to cause hepatic degeneration, and intermittent obstruction which causes cirrhosis. The important thing is that these changes do not progress sufficiently to affect galactose tolerance in three weeks, and in some cases may leave it unimpaired for longer periods up to eight weeks.



Coming to galactose tolerance in hyperthyroidism Hirose (1912) was apparently the first to demonstrate by the urinary method the impairment of tolerance which is characteristic of this condition, but the subject has not received much attention until the last decade. The first complete observations by this new method of estimating blood galactose appeared in 1940 when Althausen, Lockart and Soley, and Rundle and I obtained very similar results in cases of Graves' disease, i.e. we both found impaired tolerance in a large porportion of the patients investigated. Fig. 2 gives the average of our results in 41 patients compared with the normal. The curve is very similar to that of toxic jaundice, except that the two-hour value is lower. Unfortunately, we came to exactly opposite conclusions from these results, which Rundle and I ascribed to liver damage, and Althausen, Lockart and Soley to increased intestinal absorption. The probable explanation of this difference of opinion is that we did not pay very much attention to the

question of absorption, while the American workers did not pay very much attention to the liver.

It appears from the considerable literature on the subject that there is abundant collateral evidence on liver damage in hyperthyroidism both from autopsy material and from animal experiments. A more recent review by Lichtmann (1941) takes a similar view and instances three papers showing liver damage in about 50% of thyrotoxic patients by methods which were independent of absorption. These were the intravenous phenol-tetrachlorphthalein and bromsulphthalein tests and the Takata-Ara reaction. Haines, Magath and Power (1941) have also shown hepatic impairment by the intravenous hippuric acid test in 5 out of 6 patients. Therefore, there appears to be little doubt that liver damage does occur in a large proportion of cases of Graves' disease, but it is uncertain to what extent the increased absorption rate contributes to the results of tests done by oral methods.

SUMMARY

(1) A new modification of the galactose tolerance test in which blood galactose is estimated at half-hourly intervals after oral administration of the sugar has been performed on 24 patients with obstructive jaundice, and on 24 with toxic jaundice. The results confirm the suggestion previously made that the test is of some value in distinguishing these two conditions, provided that due attention is paid to the duration of the jaundice and to the shape of the blood galactose curve. The method appears to be reliable during the first three weeks, and may give useful information up to eight weeks from the commencement of jaundice.

(2) 17 cases of common infective jaundice (catarrhal jaundice) were included in the toxic group. All of these showed impairment of glycogenic function, suggesting that the jaundice was due to hepatic necrosis and not to biliary obstruction.

(3) The significance of the impaired galactose tolerance which is characteristic of Graves' disease is briefly discussed.

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The Electrocardiogram After Pneumonectomy

By CYRIL G. BARNES, M.D.

IN 1935 McGinn and White showed that after massive pulmonary embolism there may be electrocardiographic changes somewhat resembling those of posterior cardiac infarction, with which pulmonary embolism may be confused clinically. They believed that these changes were the result of acute right ventricular strain, and later investigators, particularly Wood (1939), paying special attention to the chest leads, showed that the cardiograms after pulmonary embolism closely resemble those of acute cor pulmonale from other causes. It seems likely from both clinical and experimental evidence that the mechanical obstruction to the pulmonary circulation in embolism is responsible for the failure of the right ventricle, although some workers postulate reflex changes in the coronary arteries as playing a major part in its causation.

The characteristic electrocardiographic pattern of acute cor pulmonale is now well recognized, and the main features may be summarized as follows (fig. 1). In the limb leads, voltage may be low, and an S wave develops in Lead I. In Lead III the Q wave is well marked, and there is inversion of the T wave with upward bowing of the RS-T interval. The RS-T interval may be depressed below the iso-electric line in Leads I and II, but the T waves remain upright in these leads, although they may be of low voltage. The most striking change, however, is in the chest leads, in which the T wave becomes sharply inverted, being most obvious in the right pectoral - right arm lead, and least marked in Lead IV-R. The changes may appear within an hour of the occurrence of the embolism, and it has been shown that they may persist for weeks.

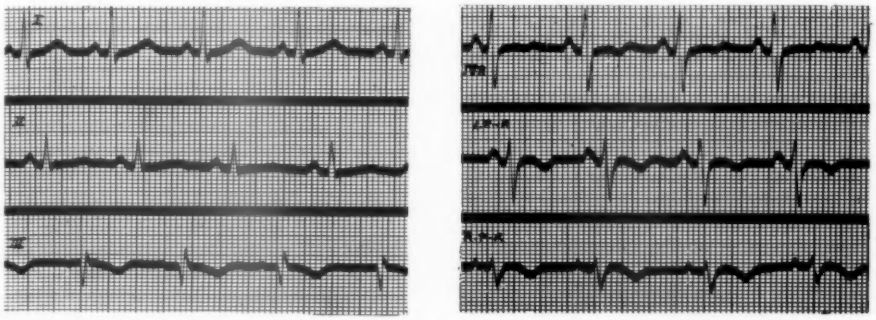

FIG. 1.—Electrocardiogram three days after massive pulmonary embolism.

Two years ago I began to take tracings whenever I was asked to see a patient suspected of having had a pulmonary embolus after operation or parturition. Since then I have taken cardiograms of eleven patients in whom the diagnosis on clinical grounds was indisputable. In only three of these was there anything approaching the typical pattern of acute cor pulmonale. Although the proportion of cases of pulmonary embolism showing these changes varies in the different series which have been published, it seemed that I was rather unfortunate in my results. I concluded that in my patients the emboli had not been sufficiently large to cause the changes, however they may be brought about, and it must be admitted that in only four of these eleven patients was the full clinical picture of massive pulmonary embolism present; in short, a combination of shock and right heart failure.

It occurred to me, therefore, that it might be possible to correlate the changes in the electrocardiogram with the size of the pulmonary vessel occluded by the embolus. It should be possible to investigate this point in patients undergoing lobectomy or pneumonectomy for pulmonary disease, taking cardiograms before, and at varying intervals after one, two or three lobes had been removed.

Through the courtesy of Mr. Holmes Sellors and Mr. Thompson of the Thoracic Surgical Unit and of Mr. Fatti, I have been able to carry this out in a small series of cases.

One might have anticipated, perhaps, that if the cardiographic changes are a manifestation of acute cor pulmonale they would not be found even after pneumonectomy, for it is generally conceded, from experimental work on animals, that from 50% to 80% of the pulmonary circulation must be occluded before acute dilatation of the right ventricle occurs. However, Love and his colleagues (1938) working on dogs were able to produce cardiographic changes similar to those resulting from experimental embolization, by constricting the main pulmonary artery until its lumen was narrowed to just under 50%, and it appeared that the changes in the electrocardiogram coincided with the dilatation of the right ventricle.

It seemed of interest, therefore, to determine whether the sudden occlusion of one main branch of the pulmonary artery in man was or was not accompanied by clinical evidence of right heart strain and the cardiogram of acute cor pulmonale.

COURSE OF THE INVESTIGATION

I began by electrocardiographing five patients who were subjected to lobectomy for bronchiectasis. In four cases one lobe was removed, and in the remaining patient both the lower and middle lobes on the right side. The cardiograms after operation differed in no way from those taken before, and I thereafter turned my attention solely to cases of pneumonectomy.

Cardiograms have been taken of seven patients who have undergone pneumonectomy, two young men aged 26 and 32 for bronchiectasis, and five older men whose ages ranged from 48 to 59 for carcinoma of the lung. One patient developed signs of pericarditis within a few hours of the operation and died from a pyopericardium. The pericarditis so confused the electrocardiogram by superimposing its own pattern that I have excluded this case from my series.

A clinical examination was carried out on each of the remaining six men before operation, and revealed no evidence of cardiovascular disease; all the patients seemed good operative risks. In every case but one, cardiograms were taken before operation and then at varying intervals after the pulmonary artery had been tied. These intervals varied with different patients. In two, tracings were obtained from the limb leads, with the patients on the operating table, a few seconds before, and perhaps half a minute after the pulmonary artery was occluded. All patients had a cardiogram taken within twenty-four hours of the operation, and most of them within twelve hours, and then tracings were taken at varying times, the latest being a fortnight after operation in one patient.

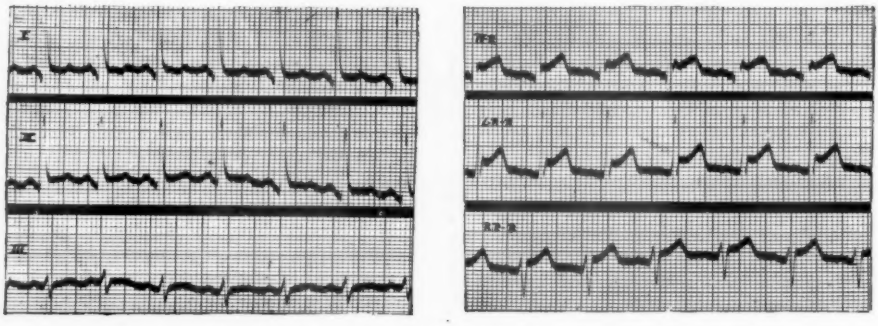

FIG. 2.—Electrocardiogram thirty-six hours after pneumonectomy.

In this way I obtained electrocardiograms at intervals in my six patients from half a minute up to fourteen days after sudden occlusion of one main branch of the pulmonary artery. Altogether a total of sixteen cardiograms were taken after operation, so that had any changes even of a transitory nature occurred it is probable that I should have recorded them.

I may state at once that in no case have I observed any cardiographic changes resembling in the slightest degree those which I have summarized as characteristic of acute cor pulmonale. Similarly, in no patient did I find signs of acute right heart failure in the form of engorged neck veins, enlarged liver, grossly accentuated pulmonary second sound, and so on.

It appears therefore that in man even after middle age, provided that the myocardium is healthy, the sudden occlusion of 50% of the pulmonary circulation does not lead to clinical or electrocardiographic signs of acute cor pulmonale, and these findings are in accord with much experimental work on dogs and other animals.

One knows that pulmonary emboli shown at post-mortem examination to be quite small, although sometimes multiple, may cause right heart failure and death, and the problem still remains whether the failure in such cases is the result of a reflex acting through the coronary arteries, or whether it is due to the myocardium, previously damaged, finding the occlusion of even a small branch of the pulmonary artery too great a mechanical strain.

In only one case were any cardiographic changes found at all after operation, but these have a certain interest in comparison with tracings taken from a case of pulmonary embolism.

A man, F. H., aged 32, was submitted to pneumonectomy for bronchiectasis of the left lung. Unfortunately, this was the one case of whom cardiograms were not taken before operation. Six hours after pneumonectomy his electrocardiogram showed the RS-T interval in the chest leads to be markedly raised and slightly so in the limb leads (fig. 2), and this persisted for four days when the last tracing was taken. At this time the other lung seemed normal, and there were no abnormal signs in the cardiovascular system;

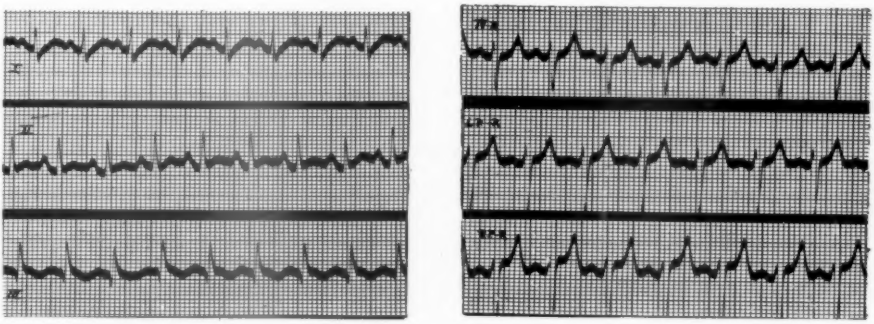

FIG. 3.—Electrocardiogram one and a half hours after pulmonary embolism.

in particular there were no clinical signs of pericarditis. He died a week later, and an autopsy was not permitted, but death was due to bronchopneumonia in the remaining lung. His cardiograms may be compared with that of another patient, a woman, who suffered a large pulmonary embolus whilst recovering from an operation for strangulated femoral hernia. The tracings were taken one and a half hours after the embolus (fig. 3), and the early changes of acute cor pulmonale can be made out in the limb leads. In the chest leads the only abnormality is the raising of the RS-T interval in the right pectoral lead where one would anticipate that inversion of the T wave would first occur. It seems possible that this raising of the RS-T interval in these two patients may represent an early stage of acute cor pulmonale before the T wave changes in the chest leads have made their appearance.

CONCLUSIONS

My findings are therefore almost entirely negative, and suggest that if, as seems generally believed, the right ventricular failure of pulmonary embolism is due to mechanical obstruction of the pulmonary circulation, then more than 50% of the pulmonary artery must be occluded to cause it, in the presence of a healthy myocardium. This means that only very large emboli, such as those that settle astride the bifurcation of the artery, or multiple smaller emboli can be expected to give the typical electrocardiographic pattern of acute cor pulmonale. This is in keeping with my findings in pulmonary embolism; two of my three cases who showed the typical pattern having died and the third being still in a

precarious state one week after the embolus. Hence the value of the cardiogram in pulmonary embolism would appear to be much less than one had hoped, although it still retains, of course, the original value attributed to it in distinguishing pulmonary embolism from posterior cardiac infarction.

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Section of Comparative Medicine

President—C. H. ANDREWES, M.D., F.R.S.

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DISCUSSION ON SWINE INFLUENZA IN THE BRITISH ISLES

F. Blakemore and A. W. Gledhill, *The Institute of Animal Pathology, Cambridge:*

ABSTRACT.—An outbreak of pneumonia affecting pigs (10-14 weeks old) was investigated; the mortality rate was low and recovery was slow. *Hæmophilus influenzæ* was recovered from half the pigs examined and the presence of a virus was demonstrated by the intranasal instillation of a filtrate of pneumonic lung. The virus was subsequently established in ferrets and neutralizing antibodies were demonstrated in the blood of convalescent pigs to the ferret-adapted virus.

Four further outbreaks of pneumonia in pigs revealed the presence of a virus and in two of these the agent was adapted to the ferret. *Hæmophilus influenzæ* was obtained from only a few of the pigs.

The lungs of pigs at a public slaughterhouse were examined for pneumonia and lesions were found in some cases. *Hæmophilus influenzæ* was recovered from three of forty affected lungs and transmission experiments with material from two lungs were made. The disease was reproduced in pigs and one of the strains was later adapted to the ferret.

RÉSUMÉ.—Étude d'une épidémie de pneumonie chez des porcs de 10 à 14 semaines, avec mortalité basse et guérison lente. L'*Hæmophilus influenzæ* a été trouvé chez la moitié des porcs examinés, et la présence d'un virus démontrée par l'instillation intranasale d'un filtrat de poumon pneumonique. Ce virus a été établi par la suite chez le furet, et des anticorps neutralisant le virus adapté au furet ont été démontrés dans le sang de porcs convalescents.

Un virus a été trouvé dans quatre autres épidémies de pneumonie porcine, et adapté au furet dans deux de ces épidémies. L'*Hæmophilus influenzæ* n'a été trouvé que chez peu d'animaux.

Des lésions pneumoniques ont été recherchées dans des poumons de porcs obtenus dans un abattoir public, et ont été trouvées dans quelques cas. L'*Hæmophilus influenzæ* a été trouvé dans trois poumons sur quarante atteints de pneumonie, et des expériences sur la transmission de la maladie ont été faites avec du matériel provenant de deux poumons. La maladie a été reproduite chez le porc, et une des souches adaptée plus tard au furet.

RESUMEN.—Se estudió una epidemia de neumonía afectando puercos (de 10-14 semañas de edad); la tasa de mortalidad era baja y el restablecimiento lento. *Hæmophilus influenzæ* se obtuvo de una mitad de los puercos que eran examinados, y la presencia de un virus se demostró por medio de instilación intranasal de un filtrado de pulmón neumónico. Se comprobó después el virus en hurones, y demostróse en la sangre de puercos convalecientes anticuerpos neutralizando el virus adaptado al hurón.

Mostraron la presencia de un virus cuatro nuevas erupciones de neumonía en puercos, en dos de las cuales era el agente adaptado al hurón. *Hæmophilus influenzæ* se obtuvo de unos pocos puercos solamente.

Se examinaron por neumonía los pulmones de puercos en un matadero público, y se encontraron lesiones en algunos casos. De cuarenta pulmones afectados *Hæmophilus influenzæ* se recojó en tres, y se efectuó transmisiones experimentales con material de dos pulmones. La enfermedad fué reproducida en puercos, y una cepa adaptada más tarde al hurón.

RESUMO.—Investigou-se o aparecimento de numerosos Casos de pneumonia em leitões de (10-14) semanas de edade; a taxa de mortalidade foi baixa e o restabelecimento foi vagaroso.

Obteve-se o bacilo hemofilo da influenza de metade dos porcos examinados e notou-se a presença de um virus, o que se demonstrou pela instalação intranasal de um filtrado do pulmão pneumonico. O virus foi depois transmitido a furões e demonstrou-se existirem corpusculos neutralisantes no sangue dos porcos convalescentes do virus transmitido aos furões.

No aparecimento de outras quatro epedemias de pneumonia em porcos, notou-se a presença de um virus e em duas delas, o agente tinha sido transmitido a furões. O bacilo hemofilo da influenza obteve-se sómente de poucos porcos.

Os pulmões dos porcos num matadouro publico foram examinados para vêr se estavam afetados com pneumonia e em alguns casos encontraram-se lesões. O bacilo hemofilo da influenza foi encontrado em trez dos quarenta pulmões afetados, e fizeram-se experiencias de transmissão com material tirado de dois pulmões. A doença foi reproduzida em porcos e um dos derivados foi adaptado depois em furões.

SWINE influenza has been extensively studied in America where it was first described by Dorset *et al.* (1922). The disease affects young pigs (10-14 weeks old), is characterized by pneumonia, and coughing and sneezing are the most prominent symptoms. The onset is sudden and recovery is rapid: the mortality is low. Shope (1931) showed that it was caused by a virus combined with *Hæmophilus influenzæ suis* and that the bacterial infection played an essential part in the ætiology of the natural condition.

An infectious pneumonia of pigs has been recognized for many years in Europe but its relationship to the American influenza has not been established. In Germany the disease (Ferkelgrippe) affects piglets 3-4 weeks old and according to Köbe (1933) it is caused by *H. influenzæ* and a filtrable virus; chronic cases of the disease are common and *Pasteurella suiseptica* is recovered from a large proportion of the pigs so affected.

Lamont (1938) produced evidence that an influenza-like disease occurs in N. Ireland and Lamont and Shanks (personal communication 1940) have studied it recently. There are no published reports of its existence in England. An infectious pneumonia is recognized by veterinary practitioners, but the ætiology of the condition has not apparently been studied. We have investigated several outbreaks and in each case have demonstrated the presence of a filtrable virus; in some herds the disease resembled the influenza as described elsewhere.

SOME OBSERVATIONS ON A TYPICAL INFLUENZA-LIKE DISEASE OF PIGS (Outbreak T/1)

An outbreak of pneumonia on an Essex farm was investigated. There was no previous history of the disease, and, although there were pigs of all ages on the premises, it affected only those 8-14 weeks old. Sneezing was the most characteristic feature and many of the pigs showed no other signs of infection. Severe cases developed symptoms of pneumonia and prostration; delirium was noticed at the height of the attack in a few.

The course of the disease was usually short but the pigs which had shown evidence of pneumonia were unthrifty for several weeks and suffered from a chronic cough. The mortality was low. Post-mortem examination revealed catarrhal changes in the nasal cavity and in most cases the lungs were also involved. The extent of the pulmonary lesions varied though it was mainly the apical, cardiac and intermediate lobes which were affected. Sections of typical lungs revealed a bronchopneumonia, with areas of collapse. There was also a peribronchitis, and in many instances the bronchioles were surrounded by a zone of small round-celled infiltration.

Hæmophilus influenzæ was recovered from three of five cases examined and the strains required both X and V factors for growth, especially large amounts of the latter (Fildes, 1923).

Pigs could be readily infected by the intranasal instillation of Berkefeld filtrates of the lungs and turbinates although the condition produced was much milder than that which resulted from the use of unfiltered lung infected with Hæmophilus. With the superimposed bacterial infection the clinical picture was not so striking as that of the field disease and sneezing was not a constant feature.

In view of the influenza-like nature of the condition an attempt was made to infect ferrets in the same way. The first experimental animal showed only a slight rise in temperature but when the material from this ferret was passed to another, acute symptoms resulted and this occurred in ten succeeding ferrets. The temperature reaction was typical of influenza and the symptoms included sneezing, with signs of pneumonia in severe cases. The ferret-adapted virus was infective for pigs. Evidence that the virus with which we had been working was closely related to that causing the natural disease was obtained by the demonstration of neutralizing antibodies in pooled samples of blood obtained from convalescent pigs on the affected farm.

EVIDENCE CONCERNING A VIRUS PNEUMONIA OF SWINE IN ENGLAND

During the winter of 1940 four selected outbreaks of pig pneumonia were investigated. The particulars relating to them can be summarized as follows:

S/1. This outbreak was described by the veterinary practitioner as being typical of a specific pneumonia of pigs which occurs in Norfolk. Pigs 10-14 weeks old were affected, signs of pneumonia were apparent but sneezing and catarrhal symptoms were not observed. The course of the disease was short and the mortality low. The lung lesions were similar to those found previously and there was also pleurisy and pericarditis. *Pasteurella suiseptica* and *Brucella bronchiseptica* were isolated from the lungs and Gram-positive bacilli from the pleura and pericardium. Normal pigs were readily infected by emulsions of lung material and the virus was adapted to the ferret without difficulty.

H/1. The disease appeared when the pigs from various sows were mixed after weaning. Some of the affected pigs died of pneumonia after an illness lasting about five days but in others the condition became chronic. Some of the pigs showed signs of enteritis, but we were unable to obtain any evidence of swine fever on the premises. Post-mortem examination revealed that pneumonic lesions of the kind found in the previous outbreaks were constantly present. In addition, some of the subjects showed an ulcerative colitis, the lesions being similar to those usually associated with Salmonella infection. Cultures of lungs from affected animals failed to reveal a constant infection; *Pasteurella, Br. bronchiseptica and diplococci* were recovered from different specimens. The infective nature was established by intranasal instillation into normal pigs and later ferrets were infected.

G/1. The general features of this outbreak resembled those of H/1 but there was no evidence of intestinal involvement. Moreover, there was a history that some of the piglets

were affected before weaning and sneezing had been observed amongst them. The lesions were confined to the lungs. *Hæmophilus influenzæ* was recovered from both the specimens examined; streptococci and Gram-positive bacilli were also isolated. Normal pigs were infected with an emulsion of lung but we were unable to transmit the disease to ferrets.

C/1. This outbreak occurred amongst pigs 10-14 weeks old which had been recently purchased. The disease caused only a low mortality but many of the affected pigs became unthrifty and were economically unprofitable. Pneumonic symptoms only were observed and post-mortem examinations revealed characteristic lung changes with pleurisy and pericarditis in severe cases. The bacterial findings were somewhat similar to outbreak H/1 but in addition *H. influenzæ* was recovered from one of the six specimens. The disease was readily transmitted to normal pigs, but despite persistent attempts we were unable to set up symptoms in ferrets or to stimulate a suggestive temperature reaction.

THE EXAMINATION OF SLAUGHTERHOUSE MATERIAL

During the winter months an examination was made of the lungs of pigs at a slaughterhouse. Pneumonic lesions resembling those which had been previously studied were found to be common and it was estimated that at least 25% of the pigs were affected. The lesions were in various stages of development and in many of the specimens resolution was complete, the areas then being sharply defined and somewhat resembling pancreas in colour and consistency. A cultural examination was made of 40 selected lungs and from three *H. influenzæ* was recovered. Streptococci of various kinds were the commonest invaders and *P. suiseptica*, *Salmonella* and Gram-positive bacilli were recovered from other cases. It was only possible to carry out transmission experiments with material from two of the specimens and the disease was readily transmitted to pigs with emulsions of both of these. One of the strains was discarded, but the other, which was passaged by the use of a filtrate, was adapted to the ferret without difficulty and has been subsequently maintained.

Discussion

Our findings indicate that an infectious pneumonia of pigs occurs in this country, and we have some evidence that the condition is not uncommon. In the first outbreak we investigated the picture was typical of influenza, and although the symptoms in the other herds were not so striking the fact that four of the recovered viruses set up the characteristic disease in ferrets indicates the necessity of studying their relationship with known influenza strains from both human and animal sources. The recovery of *Hæmophilus influenzæ* from a proportion of the field cases is a further indication of the influenzal nature of the disease. Moreover, the indefinite nature of the symptoms in pigs experimentally infected with strain T/1 virus seems to indicate that a typical influenzal syndrome may not occur in all field cases.

The disease we encountered resembled in some respects swine influenza as described in America. They both occur in pigs 10-14 weeks old but, while chronic unthriftiness was the more serious feature in four of our five outbreaks, American workers emphasize the acute nature of the disease with rapid recovery. *Hæmophilus influenzæ* was not constantly present in the field cases we examined and this organism did not appear to play a unique rôle in the ætiology of the disease since other bacteria, such as Pasteurella, were isolated from severe clinical cases. Shope has stressed the importance of Hæmophilus as a secondary invader and while we are in agreement with his views our bacteriological findings are more in accordance with those of McBryde and others (1928) who described a somewhat similar bacterial flora in American cases to that observed by us. It is interesting to note that they isolated Gram-positive bacilli from a number of pigs, which they failed to classify. The organisms of this kind which we recovered were usually associated with suppurative foci and while they appeared to be a heterogeneous group several showed general reactions similar to those described by the above workers. A further point of interest in connexion with our bacteriological findings was the recovery of *Br. bronchiseptica* which is in accordance with earlier American findings.

The lesions we found closely resembled those from cases of swine influenza in N. Ireland, which were kindly sent to us by Lamont, and we were able to set up a mild

disease in ferrets with this material, although we did not succeed in maintaining the virus by passage. Indeed, the only essential difference between the general features of the two diseases would appear to be that unweaned pigs are frequently affected in N. Ireland. The disease in Germany too occurs in unweaned pigs, and it is often of a chronic nature. For these reasons Waldmann (1933) states that it is a separate entity from that described by Shope in America, though he considers it to be due to a virus and Hæmophilus. It has been suggested by Shope and Francis (1936) that the condition in Germany is caused by prevalent human influenza virus strains and Hæmophilus and that only suckling pigs are naturally susceptible to this form of the disease. Our disease in point of age susceptibility resembled the American in four out of the five outbreaks, while in its chronic nature it resembled the European. Age-incidence may be related to the conditions under which the pigs are kept and of little importance in comparing the essential nature of the disease. Moreover, it is likely that our five strains of virus are not themselves identical and further classification of these conditions must await a closer study of the viruses concerned.

In the course of our investigation into outbreak T/1 we showed that the virus persisted in the lungs for some considerable time, its presence being demonstrated in a pig which had been ill for eight weeks. This finding is in accordance with the view of Köbe (1934) who maintains that it may be transmitted by mixing healthy pigs with the survivors of an outbreak. Waldmann (1937) is of the opinion that it spreads by droplet infection, and as a measure of control he advocates a system of management in which there is no aerial communication between the breeding pens. While the lungs of our acute cases were not affected with parasites a large number of worms (*Metastrongylus apri*) were present in the chronic condition. We were unable to obtain evidence that parasites played any part in the development of the disease. This would seem to be a matter for further investigation, however, especially in view of the fact that our colleague Dr. Lapage found 24 of a recent series of 52 normal lungs to be affected with *Metastrongylus apri*.

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Mr. R. E. Glover: Andrewes, Laidlaw and Smith (1935) found that in the sera from adults and from children over 10, antibodies to swine influenza were present as regularly as those active against the human viruses. They were unable to determine whether these antibodies were specific or nonspecific since at that time swine influenza had not been recognized in England.

In order to study the antigenic composition of these pig viruses more thoroughly an attempt was made to transmit them to mice. Dr. Andrewes and I established three strains, two from Cambridge and one from Northern Ireland. The examination of these viruses is still in the preliminary stage, and the information which has been obtained can only be regarded as complementary to the data which have already been furnished by the workers at Cambridge and in Northern Ireland.

Mice were inoculated by the intranasal instillation under ether anæsthesia of 0·05 c.c. of a supernatant fluid from centrifuged suspensions of the material under examination. The two first strains (C1 and C2) which were received through the courtesy of Mr. Blake-

more, had been isolated in Cambridge and had been adapted to the ferret, C1 having been passed through a series of ten ferrets, and C2 through three ferrets. Six mice were inoculated with a suspension of ferret lung (C1) and were killed four days later, but no pulmonary lesions were detected. A suspension of the lungs of these mice was transferred to six animals, again without visible result. In the third passage, however, one mouse showed complete consolidation of half of one lung, and one had a suspicious lesion: from this point the invasiveness of the strain became more pronounced. The second Cambridge virus (C2) behaved in a similar manner. The impression was gained that these strains were more readily adaptable to the mouse when the inoculum comprised a mixture of ferret turbinate and lung, since lesions were produced in the first passage with C1 and in the second with C2. The changes in affected mice were those of a plum-coloured consolidation with ill-defined margins which, in severe cases, affected practically the whole of the pulmonary tissues. It is interesting that these strains were apparently much less readily adapted to mice than those examined by Shope.

The material from Northern Ireland was sent in the form of consolidated lungs from natural or experimental cases in the pig. So far only one strain has been established. In this instance the inoculum, comprising a suspension of pulmonary tissue from an experimental pig, readily infected ferrets producing a typical diphasic febrile reaction. On the other hand, mice inoculated with the original material were completely refractory in spite of serial passage through five groups of six each. The strain was eventually adapted to the mouse from a mixture of turbinate and lung of the second ferret in the series, although definite lesions did not appear until the third generation. Efforts to establish other strains from Northern Ireland have not been successful. In these instances, however, the material was derived from natural cases which were regarded as typical of piglet influenza, but as it was not possible to confirm the diagnosis by the inoculation of experimental pigs it is not certain that the virus was actually present.

The three viruses mentioned above have been filtered through gradocol membranes with an average pore size of $0{\cdot}77\mu$ and have invariably proved infective for mice in dilutions ranging from 10^{-3} to 10^{-5}. Elford, Andrewes and Tang (1936) have already shown that the diameter of the Shope swine influenza particle is in the region of $0{\cdot}18\mu$, in which respect it resembles the WS virus. The Cambridge C1 strain was subjected to filtration through a series of gradocol membranes of decreasing porosity. Evidence was obtained that it was identical in size with that of the other influenza viruses.

The amount of virus in the lungs of infected mice has been determined on several occasions. In the mice in the early passage series the titre was not high, varying from 10^{-2} to 10^{-3}, but later the infectivity increased considerably, and all three strains now regularly titrate at 10^{-5} and 10^{-6}.

At present it is not possible to give more than a general pattern of the antigenic structure of these pig strains since their relationship to Shope virus on the one hand and to human strains on the other has not been precisely determined. An attempt was made to compare Shope, C1, C2 and Northern Ireland (N.I.) by serum neutralization tests in which convalescent ferret sera prepared against each of these viruses were tested in falling dilutions, varying from 1:2 to 1:1,250, against the homologous and each heterogenous strain. With the exception of the N.I. serum, which contained antibodies which were as effective against C2 as against its own virus, these sera invariably showed a higher antibody content against the homologous than against the heterogenous strains. On the whole, the British strains seemed to be more closely related to one another than to Shope, although there was some degree of cross-protection. It was found that several standard ferret sera (human strains), viz. WS, Tal., Gat., and Chr., and human convalescent sera known to be active against Shope, neutralized C1 virus to about the same extent as the Shope strain.

The fairly close relationship of Shope virus and the British strains was not altogether confirmed by vaccination experiments in mice. In the preliminary experiments mice immunized by two doses of living C1 virus were completely protected against a 1:100 dilution of C1, whereas Shope virus, in a dilution of 1:1,000, produced death or widespread lesions. This result was confirmed by a more extensive trial in which three groups of mice were vaccinated with C1, PR8 and Shope, respectively. Immunity tests gave the following results:

(1) Mice vaccinated with C1 were almost completely immune to the same strain (90%) but were only slightly protected against PR8 (8%) or against Shope (27%).

(2) Mice vaccinated with PR8 were moderately immune to the homologous strain (73%) and to C1 (82%) but showed an appreciable susceptibility to Shope (33%).

(3) Mice vaccinated with Shope were completely refractory to the homologous strain (100%) but were only partially resistant to PR8 (27%) and were completely susceptible to C1 (0%). There was some indication, however, that these results might be attributable to qualitative factors since a fairly severe test dose was given.

Shope (1939) has found that all his North American strains of swine influenza are serologically identical, or almost so; on the other hand, they stand sharply apart from most human strains. Our immunological studies are incomplete, but at present they seem to indicate that British pig strains form a less compact group than the American strains and serologically are rather different from them. It is by no means certain that they are as clearly separated from the human viruses as are Shope's strains; possibly they will bridge the gap between human and American porcine influenza viruses.

We are grateful to Mr. F. Blakemore and Mr. H. G. Lamont for sending us material.

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Dr. E. L. Taylor (Veterinary Laboratory, Weybridge): My own particular interest lies in Shope's worm-transmission theory. Evidence of the possible inoculation of microscopic or ultra-microscopic infection by parasitic worms has been of the clinical-observation type, usually without controls of any kind, and has frequently depended upon nothing more than the coincident observation of the presence of helminth parasites in a diseased host. At one time a French investigator concluded that by biting and boring into the intestinal wall, or by wounding it with hooks and suckers the majority of helminths favour the penetration of microbes. Some of the observations listed by him, however, appear to be far fetched. As an example, one account, offered as evidence, is of a fatal septicæmia traced to the presence of a single individual *Trichuris*, now generally considered to be among the most harmless of helminth parasites.

Evidence from controlled observations is less easy to find. A few years ago, with the collaboration of H. S. Purchase, I made a series of observations to ascertain whether penetrating nematode larvæ or adult strongyloid worms might assist the invasion of the animal body by bacteria from the intestine. *Bacillus anthracis* was used in guinea-pigs in one series, and in another *Salmonella suipestifer* was used in rabbits. In spite of having brought about the coincidence of pathogenic bacteria and intestine-injuring parasitic worms we were unable to find evidence of any action whatsoever on the part of the parasitic worms in assisting the bacterial invasion.

As, apart from one or two special examples such as "blackhead" in turkeys and possibly "footrot" in sheep we cannot find any proof of the transmission of *visible* organisms, we should be all the more cautious about accepting the idea of the transmission of *ultra-visible* organisms by parasitic worms.

There is, however, one very good example of the transmission of some as yet undiscovered disease organism by a parasitic worm, namely, the transmission of the so-called "salmon poisoning" of Canidæ by the trematode *Troglotrema salmincola*. This very fatal disease is transmitted to dogs, foxes, wolves, &c., by eating fish of the salmon family, infected with the fluke. There appears to be no other way in which the disease is transmitted naturally. Injection of triturated flukes produces the disease and it now seems to be

established beyond any doubt that this trematode while present in the intermediate host fish, is carrying the organism responsible for a fatal disease of dogs.

In spite of this precedent, however, in the presence of alternative explanations concerning the prevalence of swine influenza, the indefinite nature of the symptoms sometimes shown, and the possibility of animals already carrying the infection, unknown to the investigators, the lungworm theory cannot be accepted as a complete explanation.

Section of Urology

President—T. E. HAMMOND, F.R.C.S.

[*May* 22, 1941]

Forty Years' Experience of Urology

By Sir HUGH LETT, Bart., *C.B.E.*, F.R.C.S.

IT is difficult to realize the tremendous strides that surgery has made since the end of the last century, and even those of us who have seen the changes that have taken place are perhaps barely conscious of the progress that has been made. How great it is we cannot appreciate until we begin to compare the surgery of to-day with that of forty years ago and, remembering how relatively little we knew then, recall one by one the discoveries that have since been made and stand out like milestones on the road of surgical progress. But in no branch of surgery has diagnosis been brought to such a high degree of accuracy as in the diseases of the urinary tract, and when we review its history and rapid development we may well regard the time before this century dawned as the dark age of urology.

Lister laid the foundation of modern surgery, and had it not been for his great work the striking advances in urology would not have been possible. But while we acknowledge our great debt to him let us remember also what we owe to our physicists and biochemists. His work prepared the soil, but they by the results of their research sowed the seeds whence sprang new means of diagnosis, new forms of treatment, and new methods for the investigation and care of patients before and after operation. For as we look back we see that since the principles of antisepsis and asepsis were established the outstanding factors in urological progress have been the discovery of the X-rays and, later, pyelography, the remarkable developments in the cystoscope, the tests for renal efficiency and the medical treatment of urinary infections.

X-RAYS

The X-rays were discovered in 1895 and MacIntyre (1896) of Glasgow obtained the first positive radiogram of a renal calculus in the following year, but it was a considerable time before radiography became reliable. Even in 1907, one of the most prominent radiologists in New York said that in the minds of many there was considerable uncertainty as to the practical value of the X-rays in the diagnosis of urinary calculi. Many mistakes were made of both commission and omission, shadows due to other causes were attributed to calculi, while calculi of relatively slight density could not be demonstrated

and so were overlooked. These mistakes were partly due to relatively crude apparatus, but mainly to uncertainty as to the exact position of the kidney and ureter in any individual case. This generally had to be assumed, and consequently the relation of a suspicious shadow to the kidney or ureter was largely a matter of conjecture. Chastening experience showed that a dogmatic report on the X-ray examination was seldom possible, and few radiologists were inclined to commit themselves beyond saying that the shadow appeared to be in the position of the kidney or ureter and that it was probably a calculus.

Tuffier as long ago as 1897 tried to meet the difficulty by loading a ureteric catheter with a metal stylet, passing it up to the pelvis of the kidney and then having the X-ray examination made. Few surgeons, however, followed his example and there was little progress until Hurry Fenwick (1905) introduced a bougie that was opaque to the X-rays. This was a great improvement on the metal stylet and the principle was soon applied to ureteric catheters. It then became possible to demonstrate with reasonable certainty whether a shadow was or was not in the position of the kidney or in the line of the ureter. This was of great importance and much was gained, but mistakes still arose, for such a shadow was not necessarily within the kidney or ureter, it might lie behind or in front of them and be due not to a calculus but to some other cause, such as a calcareous gland. It was not long, however, before this aspect of the problem was solved by stereoscopy. The introduction of catheter pyelography in 1906 led to a still greater accuracy which reached a very high standard when intravenous pyelography was generally adopted.

The first deliberate operation for uncomplicated renal calculus was performed by Henry Morris in 1880. But at this time, and until the last century was drawing to a close, the diagnosis was based solely on clinical evidence, the most important features being the character and position of the pain and the presence of hæmaturia. The operation was therefore primarily exploratory, and in a number of cases it was negative and no calculus could be found. Sometimes the diagnosis was wrong, sometimes although the diagnosis was correct the stone was small and buried in the kidney substance, or it had passed down the ureter. Now, however, the presence and exact position of a calculus can be determined with a certainty and precision that were unknown even twelve years ago, when we first heard of the possibilities of intravenous pyelography.

It is interesting to turn for a few moments to the operative treatment of stone in the ureter. In 1892 Cabot said that practically, in adults, the lower 3-4 in. of the ureter could not be reached from in front by an extraperitoneal incision, and he suggested that a calculus in this position might be approached from behind by a modified Kraske incision with removal of the coccyx and part of the sacrum. I have seen the ureter explored through an incision in the ischiorectal fossa, while in women calculi at the lower end of the ureter were frequently removed through the vagina. It was not until 1910 that the abdominal extraperitoneal route was found to be practical, when Gibson described an operation through an incision parallel to and above Poupart's ligament. This was subsequently modified by Kidd (1913), and in 1914 Judd wrote his paper on the exposure of the ureter extraperitoneally through a mid-line incision. These papers founded the present technique of operations on the pelvic part of the ureter, but some surgeons were loth to abandon the intraperitoneal route and for a time preferred to expose the ureter by performing a laparotomy and incising the peritoneum lying over it.

PYELOGRAPHY

In its early days catheter pyelography was not devoid of risk, for collargol was employed as the opaque medium and unfortunately it led to a fatal issue in certain cases in which the pelvis was overdistended and as a result calices were ruptured and pyelovenous backflow followed. This difficulty was overcome by substituting for collargol a solution of sodium bromide or iodide which, though not quite so opaque to the X-rays, was innocuous and proved satisfactory. But though ascending pyelography proved very valuable in the diagnosis of obscure cases it was not always applicable, because it necessitates the passage of a catheter up the ureter to the renal pelvis. This is not always desirable, and the presence of a stricture or a calculus in the ureter may make it impossible. Further, a catheter pyelogram only shows the outline of the pelvis and calices when they are arti-

ficially distended by the injection of fluid from below, and it does not give a true picture of the pelvis and calices as they are being filled by the flow of urine from the kidney. The brilliant discovery of intravenous pyelography in 1929, twenty-three years later, was a great advance, and it is difficult to overestimate the important part it now plays in the diagnosis of surgical conditions of the kidney and ureter.

The modern urinary surgeon would regard an operation on the kidney as unthinkable unless either intravenous or catheter pyelograms or both had previously been made. Apart, however, from the help it affords in the diagnosis of such conditions as carcinoma, tuberculosis or hydronephrosis, pyelography has done much to throw light on cases which, otherwise, would remain difficult and obscure. Forty years ago cases of hæmaturia and renal pain which could not be explained were described as symptomless hæmaturia and nephralgia, but now, in consequence of our increased knowledge and in particular because of the assistance given by the X-rays and pyelography, these terms have largely ceased to exist.

RENAL EFFICIENCY

"Remember the other kidney." Many years ago Harold Barnard concluded a lecture on nephrectomy with these words. The warning may perhaps puzzle the young surgeon of to-day, for he accepts as a matter of course the various pre-operative tests and examinations of the second kidney, which tell him whether it is healthy or diseased, and whether it is equal to the task of performing the function of both kidneys if the first be removed. But when that lecture was given we had none of the tests for renal efficiency that are now used, radiology was in its infancy, pyelography was unknown, and death from uræmia was a very real risk. In some cases the remaining kidney was seriously diseased, in others it was atrophic, and in yet other cases it was absent and the one and only kidney the patient possessed had been removed. In order to prevent this catastrophe, many surgeons made a practice of palpating the second kidney before removing the one which was obviously diseased. Some did this after opening the abdomen, and if they were satisfied with the information they obtained they then proceeded to perform an abdominal nephrectomy. But before long this was abandoned, largely because of the risk of peritonitis. More commonly a preliminary lumbar incision was made on the sound side through which the kidney could be examined. Yet again, some surgeons, after making a lumbar incision over the affected kidney, opened the peritoneum and passed a hand across the abdomen to palpate the other. But these methods did little more than enable the surgeon to know that a second kidney was present and that it was neither grossly nor irregularly enlarged nor atrophic. Cystoscopy was of no great avail apart from revealing the orifice of a second ureter and jets of urine coming from it. We cannot wonder therefore that the first twenty-four hours after the operation were anxious ones for the surgeon, or that if he saw the patient during this time his first question was the amount of urine that had been passed.

The first tests for renal efficiency were based on the excretion of certain dyes, apart from cryoscopy, Ambard's co-efficient and others which had only a short vogue. Methylene blue was suggested by Achard and Castaigne in 1897, but it was slow and unreliable, and was superseded by indigo-carmine some six years later. This has proved of great value, and its rapid excretion and the simplicity of the test make it particularly useful when nephrectomy has to be performed in an emergency. Phenolsulfonephthalein was introduced by Rowntree and Geraghty in 1910 and has found great favour in the United States of America, but it has not been employed extensively in this country.

An important advance along fresh lines was made in 1920 when MacLean and de Wesselow announced their urea concentration test. This, in combination with the estimation of the blood urea, is of great importance in making a prognosis, particularly when prostatectomy is under consideration, and these tests have proved of very great value.

PROSTATIC OBSTRUCTION

The developments that have taken place in the treatment of prostatic obstruction make one of the most interesting chapters in the progress of urinary surgery. For many years regular catheterization had been the routine, substituted occasionally by permanent

suprapubic drainage. Catheter life, as it was called, has been strongly condemned, and it has even been stated that patients who are wholly dependent on the catheter are not likely to survive for more than two years. This is not the case, provided that adequate precautions are taken and the patients are under careful supervision. Many who possessed average intelligence and submitted to the necessary discipline lived on in good health and comfort. Sir Buckston Browne had two patients who lived to be a hundred, although for the last twenty years of their lives they passed all their urine by catheter, and in common with other urinary surgeons I have performed prostatectomy upon patients who had led a catheter life for many years whose urine was clear and free from pus. But on the other hand there are obvious disadvantages. It is very irksome for the patient to find himself dependent on a catheter and to have to perform the ritual every six hours. The prevention of infection calls for very careful supervision by his doctor in the early days, and strict obedience on the part of the patient to the instructions given to him.

There are, however, some cases in which catheter life is unsuitable or even impossible. The urethra may be a difficult one and the passage of the catheter far from easy. The patient may be clumsy with his fingers or very short-sighted. Stone may be a complication, or possibly carcimona or papilloma of the bladder, the prostate may be vascular and bleed readily, or the patient may have important attacks of intravesical hæmorrhage.

In 1893, White tentatively suggested castration as a possible cure for the enlarged prostate. This was taken up by a number of surgeons, and in 1896 Cabot collected and reviewed 203 cases. His report was very unsatisfactory, for he found that 39 of the 203 patients, 19·2%, had died shortly after the operation, real successes were few, and serious mental disturbance was not uncommon. Happily this mutilating procedure was soon abandoned.

Suprapubic prostatectomy was first performed by Belfield in the U.S.A. and McGill in this country, and later Fuller and Guiteras developed its technique, but it was not widely practised until after 1901. In this year Freyer started his campaign and by persistent advocacy and repeated publication of his results he made suprapubic prostatectomy the standard surgical treatment of the enlarged prostate in this country. But although Freyer reported in 1904 that he had operated upon 107 cases with 10 deaths the general mortality was heavy, some patients died from hæmorrhage and others from infection, but the most frequent cause of death was uræmia. Little or no consideration was given to the efficiency of the kidneys and, as we have seen, the various means of estimating it were not developed until later. Little was done to prepare the patient for the operation, and not uncommonly prostatectomy was performed during an attack of acute retention. This was remarkable, for the older surgeons who had had a wide experience of treating prostatic patients by catheterization were keenly alive to the danger of suddenly evacuating a grossly distended bladder which might have contained a large amount of residual urine for many weeks or even months.

At a meeting of the American Surgical Association in 1909 Stillman drew attention to preliminary drainage of the bladder in cases of serious sepsis, and quoted MacEwan who had drained an infected bladder through the perineum before performing perineal prostatectomy. His remarks, which were supported by Bevan, excited considerable interest. A number of surgeons began to practise the two-stage operation, notably Pilcher (1912) and Lilienthal (1912), and in 1917 Gardner was able to report that he had operated on 81 cases in this way without a death. The operation became very popular, and in some clinics it became the custom to carry out preliminary drainage in all cases.

Meantime in 1917 Pilcher emphasized the importance of decompression, or emptying the bladder by slow degrees, either by catheter or a suprapubic tube. This was quickly accepted and put into general practice, for although the mortality associated with the actual removal of the prostate had been greatly reduced, surgeons were much concerned by the large number of patients who died after the first stage of the operation before any attempt was made to remove the prostate. The procedure was greatly facilitated by the introduction of suprapubic puncture with the insertion of a de Pezzer catheter, and by the apparatus devised by van Zwalenburg (1920) or its modifications.

The adoption of decompression when called for, either by catheter or through a suprapubic puncture, and the discovery of the tests for renal efficiency, particularly those

for estimating the retention and excretion of nitrogen, stand out as landmarks in the history of prostatectomy. Other important features in its progress are certain details in technique which were gradually evolved to meet important complications. Hæmorrhage was one of these, and it led to the introduction of Pilcher's bag. Hagner had invented one three years before, in 1914, but they both had the disadvantage that the lower end of the bag dilated the compressor urethræ when traction was applied. This gave rise to some loss of control over the urine when the bladder began to regain its normal function, and both patient and surgeon were disconcerted to find that difficulty in expelling urine from the bladder was replaced by a varying degree of incontinence. Fullerton's modification, however, has overcome this difficulty. Stricture at the bladder neck was occasionally a tiresome sequel of the operation. In order to prevent it and at the same time control hæmorrhage, and also infection, Thomson-Walker (1919-20) designed his open operation, and finally Harry Harris (1928, 1929) of Sydney described the one which gave such remarkably good results in his hands. The latter is a great advance on previous operations and as its technique is mastered it attracts an increasing number of supporters because of the ease and rapidity of the patient's recovery and also perhaps because it accords more closely with the art of modern surgery.

Another minor point in technique, but one which has proved of great value, is the preliminary ligature of the vas on each side. This little operation when performed accurately eliminates the possibility of epididymitis which, apart from the pain and discomfort to which it gives rise, may prove a serious complication in old and feeble subjects.

This brief review of the history of prostatectomy would be incomplete unless it included a reference to resection by diathermy. In skilled hands this has proved particularly useful when the prostate is small or when the obstruction is caused by a middle lobe. But in this country suprapubic prostatectomy remains the operation of choice when the gland is much enlarged.

THE CYSTOSCOPE

In the early part of this address I referred to the dark age of urinary surgery. The expression is perhaps a not unfair description of the days before the X-rays were discovered or before radiology was in its stride, when cystoscopy was limited to a few pioneers and the cystoscope itself was regarded by many surgeons, not without some justification at that time, as a dangerous toy.

It was not until 1898 that the cold lamp was discovered, and it did not come into general use until some years later. Great care had to be taken to prevent a burn and the subsequent ulceration of the bladder which would occur if the lamp of the cystoscope were allowed to remain in contact with the bladder wall for any length of time. Other improvements followed one by one. The advent of the irrigating cystoscope was a great boon, for until then the bladder had to be washed out through a catheter. This often meant the repeated withdrawal and reinsertion of the cystoscope, particularly in cases of hæmorrhage or when turbid urine was descending from one or both kidneys. In these circumstances a satisfactory view of the bladder could only be obtained with great difficulty and the expenditure of much time and patience, and sometimes not at all. The double catheterizing cystoscope, the operating cystoscope and finally the combined cystoscope and posterior urethroscope were outstanding achievements. In the meantime great progress had been made in the lenses and the optical system generally, with the result that a far clearer definition and a wider field were obtained. Thus by gradual steps the modern cystoscope has been evolved, and it is difficult for those who did not experience the difficulties of cystoscopy and the limitations of the cystoscope in former days to understand fully the progress that has been made.

One of the greatest triumphs in the history of bladder surgery was the destruction of vesical papillomata by diathermy, which was introduced by Beer in 1910. Until then the only means of treating them was by performing a suprapubic cystotomy, and twisting them off if they had a pedicle or excising the part of the bladder mucosa to which they were attached. The substitution of diathermy through the cystoscope for a suprapubic operation was a tremendous advance. How great it was can only be realized by those who

saw these cases when the only method of treating recurrences was by further operations, whereas now all that is necessary is a simple treatment which can be given in the consulting room or the out-patient department. Indeed, if a recurrence were seen in an early stage, it was often left until it became of some considerable size because nothing short of a further suprapubic operation could be done. I remember one patient who had already been operated upon no less than nine times by different surgeons, and needless to say her case was complicated by a large incisional hernia.

Before leaving the bladder a brief reference must be made to Coffey's work on the transplantation of the ureters into the pelvic colon, and more particularly perhaps to its importance in relation to malignant disease of the bladder, and its value both as a preliminary to total cystectomy and as a palliative when the growth is too advanced for a radical operation. As an example of its success in the latter condition reference may perhaps be made to the case of a woman from whom I had removed the right kidney two years previously for calculous pyonephrosis. She returned with a rapidly growing carcinoma of the bladder which caused intense frequency and pain on micturition with hæmaturia. A radical operation was out of the question, but transplantation of the left ureter into the pelvic colon gave her complete relief until her death six months later. A point of special interest was the great dilatation of the ureter which, owing to obstruction by the growth, was an inch in diameter, yet there was no evidence of an ascending renal infection after the operation, and convalescence was entirely uneventful. I mention this case because it was the first in which I had performed Coffey's operation, and, remembering the pain and distress which are associated with the final stages of carcinoma of the bladder, I was profoundly impressed by the comfort it gave to this patient and her gratitude for what had been done.

THE URETHROSCOPE

I do not propose to dwell on the development and increasing use of the posterior urethroscope, or on its importance in the diagnosis and treatment of certain conditions, but it is not possible to conclude this short address without referring in some detail to the anterior urethroscope. One of the considerable changes that has taken place in hospital practice during the last forty years is the reduction in the number of patients who present themselves with strictures of the urethra that are severe and almost impermeable or associated with important complications. Reference to the records of the London Hospital shows that during the year 1897 no less than 50 cases of stricture were operated upon, 45 by internal and 5 by external urethrotomy, but in 1937 there were only 4, all treated by internal urethrotomy. Even more striking perhaps are the records of cases of perineal abscess and extravasation of urine. In the former year there were 19 cases of perineal abscess and 6 of extravasation, in the latter there was one solitary case of perineal abscess. In addition to the above, 27 cases were treated by dilatation under an anæsthetic in 1897 and 16 in 1937. These figures are very remarkable, and as the great majority of strictures are due to gonorrhœa we must go back forty years or more and consider the treatment of gonorrhœa in those days. It was limited almost entirely to drugs and local injections of astringent or antiseptic lotions by a hand syringe. It is not surprising therefore that a considerable number of patients were uncured, and we can sympathize with Ricord's remark that he pictured hell as a place where he was surrounded by patients suffering from an uncured gleet. Metal dilators were used occasionally in intractable cases, if the patient were sufficiently persevering to continue his attendance; otherwise no instrument was passed. After a varying length of time many patients gave up all treatment and did not come under observation again until they began to find difficulty in micturition, or retention or other complications had supervened.

Urethroscopes in those days were primitive and urethroscopy was practised by very few, and I may add that on not more than three or four occasions during my time as a dresser and house-surgeon did I see one used in the hospital, either in the out-patient department or in the operating theatre.

It was only when the urethroscope was modified by Wyndham-Powell to allow air-distension that it became of real value. Then it became possible not only to diagnose

and treat with far greater accuracy local lesions such as infected follicles, but to discover areas of local infiltration which limited the expansion of the urethra under air-distension, and treat them by full dilatation with a Kollmann dilator. If such an area is allowed to remain untreated, it becomes the precursor of a fibrous stricture, but given appropriate treatment it will disappear and no stricture will follow. The value of the urethroscope in this respect was summed up by Frank Kidd who said that with this instrument the course of a stricture could be followed from its birth until at the hands of the Kollmann dilator it met its death. In this way the urethroscope has played an important part in the reduction of the number of strictures seen to-day.

If we turn to the complications, perineal abscess, urinary fistulæ, and extravasation and cellulitis, we find another explanation, that of infection and sepsis, and in these cases it is by no means necessary that the stricture should be so tight as to be almost impermeable. Although forty years ago the principles of antisepsis and asepsis were generally accepted, they were not always strictly observed even in the operating theatre, and they were sadly neglected where the bladder and urethra were concerned. Catheters and bougies were kept in a wooden box and often enough the only preparation they had before use was a brief bath in a solution of boric acid. The senior surgeon for whom I dressed was accompanied on his visit to the wards by a theatre attendant who carried in front of him, suspended by a strap round his neck, an assortment of instruments on a wooden tray covered by green baize, not unlike the pedlar of former times. Among those instruments were steel dilators, and they were picked up and passed into the bladder without any form of antiseptic preparation. Boric acid was the only drug in use as a urinary antiseptic, and it is not surprising that urinary fever and cystitis should have been rife.

When we look back on those days and the scanty regard that was paid to surgical cleanliness we find a ready explanation for the cases of perineal abscess and extravasation of urine and cellulitis that so frequently occurred.

The treatment of the urethra to-day is very different. Adequate precautions are taken against infection, the urethra is carefully irrigated, and every instrument introduced into it is sterilized. Instances of urinary fever are very rare in relation to the large number of cases now treated in urological clinics and out-patient departments, and the fact that so much instrumentation can be done without ill-effects is a striking testimony to the progress that has been made during the last forty years.

Little reference has been made to internal medication and the use of urinary antiseptics in the treatment of infection and its prophylaxis as they have been discussed recently by this Section, but it is hardly necessary to emphasize their value and the importance of their contribution to the general advance that has been made in urology.

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Section of Anæsthetics

President—H. N. WEBBER, B.Ch.

[*May* 2, 1941]

The Relationship of Nitrous Oxide Anæsthesia and Anoxia

By K. C. McCARTHY, M.D.

Anæsthetist to The American Hospital in Britain, Ltd.

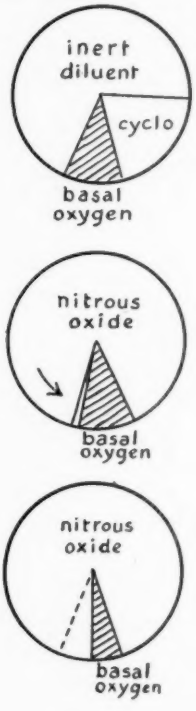
NITROUS OXIDE and oxygen has been successfully used for general anæsthesia for many years. The pleasant induction, rapid loss of consciousness, flexibility of control, freedom from vomiting and salivation, speedy recovery, and lack of complications have given it great popularity for all types of superficial and minor operations and for many major procedures as well. Lately, however, particularly in America, nitrous oxide has been vigorously attacked on the grounds that its administration is accompanied by so much anoxia that its use should be abandoned.

A formidable mass of evidence has been accumulated. Lowenberg (1936) and his associates at the University of Michigan, Schreiber (1939) at Detroit, Courville (1936) at Los Angeles, and workers at Johns Hopkins Hospital (Ford *et al.*, 1937), Henry Ford Hospital (McClure *et al.*, 1939) and others (O'Brien and Steegman, 1938; Brown *et al.*, 1938; Stewart, 1938) have all published papers presenting similar aspects. Series of deaths under or following nitrous oxide anæsthesia have been presented. The pathologic pictures have been similar, and have been characterized by extensive capillary hæmorrhage in many organs but especially of the cerebral vessels, and by œdema of the brain. Cases which have survived the anæsthesia but failed to regain consciousness have exhibited all the symptoms of decerebration with its accompanying spasm and rigidity; convulsions were common, and death occurred in a few days from pulmonary congestion and vasomotor failure. There were similar pathologic findings of diffuse cerebral capillary hæmorrhage in these later cases, but in addition, there were now areas of degeneration in the cellular layers of the cerebral hemispheres and lenticulate nucleus. Less severely damaged patients who survived had various degrees of mental impairment, ranging from complete idiocy to transient confusion and loss of memory.

Lowenberg has advanced the theory that there is something specific in the manner in which nitrous oxide attacks the cerebral cortex and claims that the lesions produced cannot be duplicated by other means. Other workers do not support this hypothesis and, pointing out the great similarity between this pathologic picture and that produced by various forms of asphyxia, including carbon monoxide poisoning, have felt that anoxia was the cause. Even Lowenberg cannot distinguish anoxia from nitrous oxide poisoning when he has no history of the case. Similar lesions can be produced in animals by anoxia; therefore, it seems to be proved that while nitrous oxide has no directly toxic effect it may sometimes produce a severe or even fatal cerebral necrosis by an accompanying anoxia. Is it possible that this danger might be present in every administration of nitrous oxide? Is anoxia necessary for nitrous oxide to produce its anæsthetic effect?

Nitrous oxide is by far the mildest and least toxic of the common general anæsthetics (fig. 1). This is one of its advantages, for practically no disturbance of bodily function is produced, but it carries with it the serious disadvantage that when enough nitrous oxide is introduced into the patient to produce the required depth of anæsthesia, there may not be enough room for sufficient oxygen to maintain bodily function. Many years ago Paul Bert (1878, 1883) carried out his classic experiments to prove that nitrous oxide was actually an anæsthetic drug and that its effects were not solely caused by asphyxia. By increasing the pressures under which the gases were inhaled, he showed that it was possible to have complete anæsthesia without oxygen shortage. By thus increasing the

partial pressures, he produced a condition opposite to that found in high altitudes. Here the aviator gets less oxygen, not because the percentage in the atmosphere is less, for it is the same as at sea-level, but because its partial pressure is reduced and his circulation thus absorbs less. Under increased pressure Bert's animals could still be maintained in good anæsthesia with nitrous oxide even though their oxygen intake was more than double that considered necessary under ordinary conditions and well above atmospheric concentrations. The effects of nitrous oxide inhalation are much more rapid and pronounced than those produced by inhaling an indifferent gas like hydrogen or helium. That nitrous oxide has specific effects apart from anoxia can be confirmed by comparing the effects of inhaling a mixture of 80% nitrogen and 20% oxygen (ordinary air) with a similar 20% oxygen - 80% nitrous oxide mixture.



(*a*) Cyclopropane, a powerful agent, permits considerable dilution.

(*b*) Nitrous oxide being weaker allows no dilution, and if sufficient is given for deep anæsthesia a reduction in the available oxygen may result.

(*c*) Morphine, by reducing the demand for oxygen, permits us to give more nitrous oxide, producing deeper anæsthesia without oxygen shortage.

FIG. 1.

Henderson and others have lately thrown doubt on Bert's experiments, claiming that only analgesia and not true anæsthesia was obtained. They have pointed out that in unprepared animals to produce real anæsthesia it is necessary to have a concentration of 95% nitrous oxide, which cuts down the oxygen to a dangerous degree, and that clinically it is impractical to administer the gases under increased atmospheric pressures. While this is true, nitrous oxide is never given for prolonged or deep anæsthesia unless the subject has the protection of morphine, which has been shown by Barbour (1936) to allow perfect anæsthesia in the experimental animal with 15% oxygen following the administration of as little as 15% of the M.L.D. (minimal lethal dose). The protective action of morphine seems to be due to its depressing effect on the metabolic rate, which McKesson (1925) has demonstrated is reduced 10% for ¼ gr. of the drug. Lessening the oxygen consumption of the patient allows us to give more nitrous oxide while maintaining the oxygen at basal levels.

Clinical experience in the administration of nitrous oxide furnishes abundant additional evidence that good anæsthesia may be maintained with oxygen, not only above the basal level for the subject, but commonly above even atmospheric concentrations. Barbour in reviewing the evidence on this subject concludes: "It is clear to-day that the anæsthetic action of nitrous oxide is totally independent of asphyxia, although it may lead to the latter condition."

Even those who support the anæsthetic action of nitrous oxide agree that its effect is much enhanced by anoxia. Anoxia is helpful only because reducing the oxygen makes it possible to increase the amount of nitrous oxide in the anæsthetic mixture. As has been mentioned, by decreasing the demand for oxygen, by lowering the metabolic rate, we can increase the amount of the gas to effective concentrations without anoxia. Clinical evidence lends this additional support. All who are familiar with its administration know how easy it is to anæsthetize those with low metabolism, such as the aged, cachectic, and those under the influence of depressing drugs. On the other hand, those with a high oxygen consumption, like thyrotoxics, athletes, and febrile patients, are especially difficult.

Evidence has been presented to show that the anæsthetic effect of nitrous oxide is not produced by and need not be accompanied by anoxia. How do we explain all these cases that have been cited previously where there can be no doubt anoxia produced serious neurologic complications? We believe that every one of these cases can be laid to technical

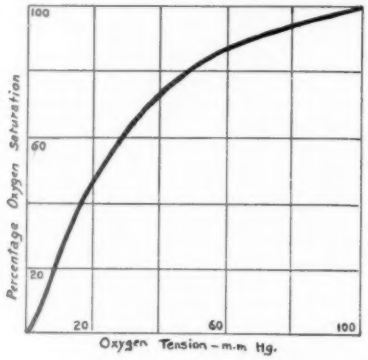


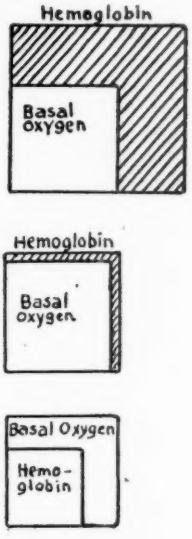
FIG. 2.—Dissociation curve of oxygen.

error in the administration. A safe oxygen level must be maintained at all times or nitrous oxide ceases to be a mild innocuous agent and produces liver damage, acidosis, and other severe constitutional disturbances, as well as the neurologic sequelæ that have been mentioned.

Should the oxygen concentration always be maintained at the atmospheric level, that is 20%? Wouldn't this always prevent anoxia? We do not think that it would. Many times patients have been encountered in whom a mixture containing even 20% oxygen and 80% nitrous oxide constituted an overdose of nitrous oxide, and the mixture had to be diluted with oxygen to 30, 40, or even 50% oxygen before signs of fourth stage anæsthesia could be avoided. Those in shock, severe anæmia, and toxic and cachectic states generally need close observation to prevent overdosage. At other times very inefficient anæsthesia would result if no more than 80% nitrous oxide could be given, and it is safe, in the average case, to reduce the oxygen considerably below ordinary atmospheric concentrations and still maintain basal oxygenation. For example, the Henderson-Haldane (Best and Taylor, 1939) expedition to Pike's Peak reached an elevation of over 14,000 ft. where the atmospheric pressure was only 450% mm. of mercury. At this pressure there was only 60% of available oxygen compared with sea-level, yet no serious symptoms were experienced, for the hæmoglobin was found to be 88% saturated with oxygen, only a 7% loss. This is due to the character of the dissociation curve of hæmoglobin, which tends to main-

tain its oxygenation in the face of reduced partial pressures of the gas. This compensation seems to be accomplished mainly by hyperventilation; however, this hyperventilation further assists by lowering the blood carbon dioxide, which in turn increases the oxygen carrying capacity of the hæmoglobin by the so-called Bohr effect (fig. 2).

Though the amount of oxygen may be reduced considerably below atmospheric levels in the normal patient, it is important that there should be enough at all times to carry on all essential functions of the body. This basal oxygen consumption could be found by determining the basal metabolism of every patient pre-operatively. Unfortunately, there are certain practical disadvantages to this plan, and furthermore, we are not sure that this basal oxygen determination would be correct for the day of operation, altered as it must be by nervousness or sedation.



(*a*) Plethoric type, much cyanosis without oxygen shortage. Much hæmoglobin is unsaturated with oxygen.

(*b*) Normal type, basal oxygen almost completely saturates the hæmoglobin, and but little cyanosis results.

(*c*) Anæmic type, impossible to produce cyanosis without reducing oxygen much below basal levels.

FIG. 3.—Cyanosis.

It is not true to say that as long as no cyanosis develops there is no anoxia. Cyanosis varies with different patients, is subject to considerable individual interpretation, and merely represents a certain degree (about 10%) of oxygen desaturation of the hæmoglobin (fig. 3). Therefore, if the amount of hæmoglobin is small, it may still be completely saturated by an amount of oxygen that may be quite insufficient for the requirements of the patient. In fact, if the hæmoglobin is below 30% cyanosis is impossible no matter how much the oxygen may be reduced. On the other hand, a plethoric individual with a high percentage of hæmoglobin will show marked cyanosis with an oxygen deficit that is quite insignificant. Therefore, no reliance is placed on cyanosis as a measure of anoxia, though if the technique is good, deep cyanosis will be rare after induction has been completed.

The following are regarded as signs of physiologic anoxia, and if any of them should appear more oxygen is supplied immediately:

Respiration: The breathing should be absolutely regular and automatic. Should irregularities such as Cheyne-Stokes' breathing, prolonged gaspy expirations, "cogwheel" breathing, or other forms of periodic respiration develop, more oxygen is needed. Periodic breathing is a common sign of oxygen deficiency observed in high altitudes.

Pulse: A rapid pulse-rate (above 100) is considered evidence of oxygen deficiency provided that there is no other obvious cause. The heart is very sensitive to lack of oxygen, as it does not have the ability of skeletal muscle to incur a large oxygen debt for it must continue to work without resting.

Blood-pressure: A blood-pressure falling below 100 systolic with a corresponding decrease in pulse pressure should always be regarded as a sign of anoxia. A similar picture may be produced by surgical shock, but it is easy to differentiate one from the other by the therapeutic test of increasing the oxygen. If anoxia is present there will be an immediate return of the blood-pressure to its normal level. This is often seen before the effect of anoxia on the circulation produces an increase in pulse-rate, and must be looked for constantly.

If we are to prevent anoxia during the administration of nitrous oxide certain precautions should be observed. Great care must be used if anoxia is already present lest we increase it. Where there is an obstruction to respiration and the patient is having difficulty in obtaining sufficient oxygen we must not curtail it further. It must be remembered that where there is limitation of free respiratory motion, such as the prone, or Trendelenburg position, with empyema or pneumothorax, there will be a decrease in ventilation even though there is no gross respiratory obstruction. In congestive heart failure or shock there is a stagnant anoxia that might be increased by too great a reduction in the oxygen intake. In hæmorrhage or anæmia where there is a reduction of hæmoglobin resulting in a loss of the oxygen-carrying capacity of the blood, more oxygen must be given. All these conditions require the maximum amount of oxygen.

Among general rules for the prevention of anoxia, one must insist on sufficient premedication to reduce the oxygen demands of the patient. This is of great importance and should always be followed unless the operation is to be very short indeed. Of course, the patient should be carried in the lightest plane of anæsthesia possible at all times. If it is impossible to maintain the correct plane of anæsthesia without signs of anoxia, one should never hesitate to supplement the nitrous oxide with some more powerful agent.

There is a real danger that serious complications may be produced by an anoxia incident to nitrous oxide anæsthesia. This is always an indication of technical error that may be avoided by proper care in administration and by close observation of the patient for signs of oxygen want.

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The Clinical Manifestations of Oxygen Lack

By E. A. G. GOLDIE, M.B., B.Ch.

THE type of oxygen lack, of which the effects are briefly described, is that produced by lowering the alveolar partial pressure of oxygen from its normal ground level value of about 100 mm. of mercury either by ascent in an aircraft or by decompression in a chamber.

The effects of decompression anoxia vary according to the rate of onset; this may be rapid, as when added oxygen supply is withdrawn suddenly from an individual at a height where the partial pressure of oxygen in atmospheric air is insufficient to support life; or of longer duration, as in an ascent to a height of 25,000 feet breathing atmospheric air.

In the former case the fall in blood saturation is immediate and may reach levels producing unconsciousness within 30 seconds; on restoring the oxygen supply the saturation rises at first rapidly, rising from 55% to 75% after the first deep inspiration of oxygen, and thereafter more slowly, taking some minutes to return to normal level. Subjectively, there is a remarkable lack of appreciation of the severity of the anoxia and it is common for a subject who has been fully unconscious to be quite unaware after recovery that he has been more than slightly anoxic. Fall of oxygen saturation is accompanied by cyanosis, flushing and rise of pulse-rate; there is very little change in respiratory depth or rate, and unconsciousness is preceded for some seconds by twitching of the limbs which develops into severe jactitation.

Anoxia of slower onset and less severe degree is accompanied at first by a feeling of uneasiness and restlessness. At saturations of 80% a change in behaviour becomes obvious; the subject fidgets, becomes irritable and will not co-operate in simple experimental procedures. There is a considerable impairment in the performance of simple mental tasks, such as making calculations or reading codes; at the same time the subject is convinced of his good condition and that he is carrying out his tasks with skill and accuracy, and when his mistakes are pointed out he often becomes abusive and accuses the observer of miscounting his scores. The handwriting forms an excellent index of the degree of anoxia, and after recovery is a convincing proof to the subject of his incapability while anoxic, which otherwise he finds difficult to believe. The absence of self-criticism engendered by oxygen lack has, of course, important practical applications; it is necessary that the pilot should not be allowed to use his own judgment as to when oxygen is necessary, as he is unable to recognize the symptoms of anoxia owing to his euphoria and may thus defer taking oxygen until his performance has fallen so far as to have disastrous results. In some individuals a period of excitement may occur during which they become hilarious and even violent; the appearance of this stage is determined by duration of the period of anoxia. The heart-rate usually rises and may reach 140/min. before consciousness is lost; respiration is quiet, in contrast to the anoxia produced by breathing nitrogen-oxygen mixtures, when the ventilation rate usually increases at once; this appears to be due, in part at any rate, to the fall of alveolar carbon dioxide which occurs at altitude.

I wish to thank Air Marshal Whittingham, Director-General of Medical Services, Air Ministry, for permission to publish this short paper and to demonstrate the anoxia meter.

Group Captain G. STRUAN MARSHALL said that he had frequently observed in both sudden and gradual anoxia a pronounced falling-off in the photosensitivity of the eye; this was sometimes noticed in its onset, but more often, when full oxygenation is restored, as a sudden increase in the apparent lighting of the chamber. The jactitation to which Dr. Goldie had referred was sometimes seen to have a mental factor: on one occasion, mentioned in a paper read by Sir Leonard Hill before the Royal Society (*Proc. Roy. Soc. London, s.B.*, 1934, **115**, 298), which was an important contribution to this question, the subject while breathing pure oxygen at 43,660 feet (118 mm. Hg) was ashy-grey, jactitating and on the point of collapse, and was brought very quickly down to 42,000 feet (128 mm. Hg); he then recovered enough to be able to write, in block letters, the words DIMMING OF LIGHT (or possibly SIGHT). What he actually wrote was DIMMIMIMIIIGING OF S(?)IMMING OF (?)IGHT. The indistinctness of the characters shown as (?) suggests some degree of mental confusion between the almost equally probable words SIGHT and LIGHT.

Another observation bore on Dr. Goldie's remarks about amnesia after sudden anoxia; the speaker had been in a large decompression chamber in charge of an experiment to determine the efficacy of a certain method of oxygenation at 35,000 ft., when a sudden emergency caused him to remove his own oxygen apparatus to go to the aid of a second subject. When the speaker recovered from the inevitable anoxic unconsciousness he realized that he was solemnly holding his patient's wrist and gazing at a stop-watch, but the arm holding the latter was oscillating so much that he could not possibly have read the watch. He was later informed that he had walked about the chamber, attentively "adjusting" all the oxygen delivery sets in the chamber (and adjusting them all wrong), but he had no memory of any such act. Examples of this automatism, resembling somnambulism, were quite frequently encountered in the "anoxic dawn," but this one would suffice as an illustration.

Spinal Anæsthesia with Heavy Percaine

By Frankis T. Evans, M.B.

For some years it was my practice to use novocain crystals for low spinal work in operations about the anus, and I found it very satisfactory in a dosage of as little as 25 mgm. dissolved in 1 c.c. of C.S.F. For upper and lower abdominal operations, however, it did not prove so satisfactory, as it was found that there was a very profound fall of blood-pressure even when moderate dosage was employed (150 mgm. in 2·5 to 3 c.c. C.S.F.). This fall of blood-pressure was not just a manometric phenomenon, but was accompanied by systemic disturbances; the patient looked ill and pinched. Pallor was marked, and vomiting was also frequently a feature. All this in spite of a preliminary injection of ephedrine 1·5 gr. subcutaneously. The other very real drawback was the time factor, for we seldom obtained more than one hour of really satisfactory anæsthesia. The Howard Jones method of light percaine was tried and given up in favour of the Etherington Wilson technique, which necessitated the patient assuming the sitting posture. The percaine was injected at a temperature of 105° F. and the patient was placed in the Trendelenburg position after a definite time interval, usually fifty-five to sixty seconds after commencing injection. This method proved awkward when dealing with the unconscious patient, and necessitated at least two helpers to keep him in position during the injection. Thus it was decided to seek a more convenient method, and we turned to heavy percaine. This technique is simple, safe, and easily controllable, for the unconscious patient can be quickly turned on to his side for the spinal injection, and as easily turned back to the dorsal posture, and the table tilted to the requisite Trendelenburg position. This routine has now been in use for some years, and I have never regretted adopting it. Very little seems to have been written on the subject of heavy percaine, and I have only been able to find one or two references. There was a paper by Silverton (1934) and some correspondence in the *British Medical Journal* (Boston, Durrans, and Gautier-Smith, 1939).

Percaine, whose anæsthetic properties were discovered by Karl Meischer, is a quinoline derivative, and is not related to the cocaine or novocain group. Its full name is butyl-oxycinchoninic acid di-ethylendiamide hydrochloride, and it is readily soluble in water. As percaine is readily precipitated in the presence of alkali, it is as well to add a drop or two of dilute hydrochloric acid to the water in which the syringes are rinsed preparatory to making the spinal puncture. The heavy solution is put up in ampoules of 3 c.c. It consists of 1:200 percaine in 6% glucose, and the specific gravity is 1·024 at 15° C. Thus the density is the same as the stovaine glucose solution, which was 5% stovaine in 5% glucose. The specific gravity of cerebrospinal fluid varies between 1·004 and 1·008 in the healthy patient.

Technique of Injection

For low spinal work, i.e. for operations upon the anus or bladder neck, the sitting posture is used so as to limit the area of anæsthesia. The aim is in all cases to give the minimal requisite dose and no more. In other words it is quite wrong to obtain anæsthesia of the legs when all that is required is insensitivity of the anus. In order to ensure this, we regulate the posture and limit the dose. Now in this hunt for minimal dosage we find that the dose required in the case of fistula is not adequate for the urethra. The nerve supply of the anus is S. 3 and 4 and that of the neck of the bladder is S.1 and 2, so that a slight variation of technique is required depending upon which particular area is the site of operation.

For operations upon the anus, such as fissures, fistulas and piles, the patient is placed in the sitting position, the feet supported upon a stool, the elbows on the knees and the head in the hands. This ensures that the spine is fully flexed, thus enabling an easy spinal puncture. The skin is prepared with spirit, care being taken not to allow any of this to run down between the natal cleft; towels are applied, and a skin wheal is raised between the spines of lumbar 3 and 4—that is to say in the 3rd space. The syringe is filled with 2% novocain, of which some 2 c.c. are injected subcutaneously and deep into the interspinous ligament. The spinal puncture is made with a needle of fine gauge (1·2 mm. diameter), the point of which has a 45° bevel. This ensures an easy tap, and also avoids the likelihood of the point being situated partly inside and partly outside the theca, thus giving rise to uncertain and imperfect anæsthesia. The puncture having been made, care is taken to be sure that the fluid can be aspirated freely. If the fluid does

not flow easily into the syringe, the needle should be rotated slightly until it does. The syringe is now charged with ½ c.c. of heavy percaine, is attached to the needle, and C.S.F. is aspirated into the syringe up to the 1 c.c. mark. Now we have in the syringe a mixture of percaine 0·5 c.c. diluted with ½ c.c. of C.S.F. This 1 c.c. of total fluid is then injected into the theca, not quickly and forcibly, but not unduly slowly; the syringe and needle are then withdrawn in one piece.

For operations upon the bladder, such as cystoscopy, per-urethral resection and fulguration, the same technique is followed. But in this case the dose of percaine is increased to 1 c.c., there is no admixture of C.S.F., and the injection is made in the 3rd space. It must be emphasized that in bladder work the injection must be made in the 3rd space and not in the 4th. (In the case of the patients who have a long lumbar spine, I give the injection for urinary cases in the 2nd space.) The patient is then made to sit bolt upright for two minutes, at the end of which time he returns to a recumbent position. It is important at this stage to see that the table or trolley is truly horizontal in order to limit the anæsthesia. There is, of course, no interference with the blood-pressure under these conditions. It is possible, I am told, to obtain anæsthesia for anal surgery by the use of a smaller dose, such as 0·3 c.c. of percaine—but I have not yet tried this. Anæsthesia is complete in five minutes.

Medium spinal anæsthesia.—By this I mean anæsthesia sufficiently high for operations to be performed on the lower abdomen, but with no guarantee of anæsthesia in the upper abdomen, i.e. anæsthesia to dorsal 10. In this case the patient is placed upon the side in the usual position, with the knees drawn up and the head well flexed. Puncture is made in the 3rd space, and C.S.F. is aspirated into the syringe just to see that the fluid flows freely. 1·4 c.c. of percaine is then drawn up into the syringe and is then introduced into the theca. The patient is immediately turned over on to his back with the knees and thighs flexed, and a Trendelenburg position of 5° immediately assumed.

High spinal.—For anæsthesia up to thoracic 6, that is to say, for operations in the upper abdomen such as cholecystectomy and gastrectomy, we use 1·6 c.c. of heavy percaine, which is expanded by the addition of 0·2 c.c. of C.S.F. to 1·8 c.c. total. This is immediately introduced into the theca. The needle and syringe is withdrawn, knees and thighs flexed as before, and a 5° Trendelenburg position assumed.

Premedication.—In actual practice we have two methods of premedication. In the first we use nembutal with omnopon and scopolamine, and in the other pentothal and gas-oxygen is administered. In the first instance the patient is given omnopon gr. ⅓, scopolamine gr. $\frac{1}{150}$ hypodermically one hour before operation, together with nembutal gr. iii orally. This is eminently satisfactory for cancer patients, as they come to the theatre so drowsy that they do not seem aware of their surroundings. (It is unusual to need any nitrous oxide in these cases.) On the other hand some patients wish to be completely asleep, and in these cases we use omnopon gr. ⅓, scopolamine gr. $\frac{1}{150}$ hypodermically, half an hour before operation. The anæsthetist then applies two pairs of rubber gloves and administers to the patient 0·5 to 0·7 grm. of pentothal intravenously. The patient is then rapidly turned upon his side, a nurse pulls off the top pair of rubber gloves, without soiling the under pair, and the anæsthetist is thus enabled to perform his spinal puncture without delay or need for washing up afresh. This procedure is eminently satisfactory, and has now been used for some years.

In one hundred consecutive cases at St. Mark's of perineo-abdominal excisions of the rectum there has not been one death on the table; so that the safety of the method can be said to be reasonably proved. Indeed, I have had no deaths within twenty-four hours of operation in the last five years, though I have had a few moments of anxiety in four or five of the early cases, due to anæsthesia rising too high. This was due to too early a Trendelenburg tilt.

Blood-pressure control.—Much has been written about the control of blood-pressure in spinal anæsthesia, but I would venture to say that one is often happier in not knowing how low the blood-pressure has fallen—I would distinguish between a blood-pressure fall which is adequately dealt with by the circulatory system, and one which causes distress thereto. On the one hand we have merely a low blood-pressure and a patient who has a quiet pulse, a warm face and is apparently quite well. On the other hand there is the patient whose fall of blood-pressure has caused acute distress as exemplified in a rapid, thready pulse, pallor, pinched features and some sweating; this is the type of patient who requires intravenous therapy at once, whereas the former is of no consequence. It is reassuring to see a blood-pressure which remains steady throughout the

whole operation. This one sometimes finds even with high spinal anæsthesia, and can be explained upon the assumption that one has not anæsthetized the all-important thoracic 5, 6 and 7. The mechanism of blood-pressure fall is a debatable question, but I do not feel that any drugs—ephedrine, neosynephrine or other drugs given hypodermically—are of any use in maintaining the blood-pressure. Personally I use ephedrine in a dosage of 1½ gr. hypodermically without any real conviction that it will maintain the blood-pressure, for it does not! On the other hand "20/20", i.e. phedracine, is extremely effective intravenously for a big fall of blood-pressure. Intravenous blood, started at the correct time, is of the greatest benefit in these big bowel operations.

POST-OPERATIVE SEQUELÆ

The patient is returned to bed and is allowed one pillow only. The foot of the bed is raised upon 6 in. blocks for some eight hours, at the end of which time the blocks are removed and a second pillow is substituted. The patient is told that during this period he must not raise his head from the pillows in any circumstances.

This brings us to the cause of headaches, the bugbear of spinal anæsthesia. We do not get any less headache with percaine than with any other spinal drug. Most authorities state that headaches occur in 10% of cases; fortunately what headaches we have seen have been mild and easily controllable with veganin or rectal mag. sulph. One patient told me that he had had 25 spinal anæsthetics, and only once did he have any headache, when, somewhere about the twelth operation, feeling that he was immune, he began to sit up and look around the ward. Since that time he has been careful to keep his head flat and has had no further trouble. I have also seen spinal headache occur when there has been no spinal puncture of the theca. This occurred after an epidural anæsthetic.

Paralysis.—I have never seen a case of paralysis following spinal anæsthesia, though I have heard of them. One patient developed paresis of the arm; it was subsequently discovered that he had general paralysis of the insane and his cerebrospinal fluid gave a positive Wassermann reaction. On the other hand, I have heard of one or two cases who have complained of "blotting-paper feet".

One small point is that after low spinal anæsthesia, although the legs are fully sensitive, the soles of the feet are anæsthetic, and severe burns can arise from hot-water bottles if the nursing staff be not reminded of this fact.

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Casualty Anæsthesia in the E.M.S.

By F. BARNETT MALLINSON, M.R.C.S., L.R.C.P., D.A.

A STUDY of the literature relating to 1914-1918 shows that war surgery was much hampered by the relative crudeness of anæsthetics. Jarman quotes a 90% mortality from primary amputation through the thigh under chloroform and ether. Introduction of N_2O-O_2 halved this. To-day, intravenous anæsthesia and modern gases and machines greatly enhance the anæsthetist's power to aid the surgeon. The drugs now at our disposal fall into four groups: *Intravenous barbiturates,* such as pentothal and evipan; *gases,* chief of which are nitrous oxide and cyclopropane; *volatile liquids,* i.e. chloroform, ether, ethyl chloride and vinyl ether; and lastly *spinal analgesic drugs.*

Experience to date has led one drastically to reduce this field, especially in dealing with the more seriously wounded, for it is in anæsthetizing these that the choice of the least damaging and toxic anæsthetic often spells the difference between life and death. With the lightly wounded the choice, generally speaking, relates rather to comfort than actual risk. Chloroform, however, is always excepted.

CHOICE OF AGENTS

In deciding on the most suitable anæsthetic, the condition of the patient must be our guide. From the anæsthetist's point of view these cases may be divided into:

(1) *Immediate cases.*—These resemble road accidents in many ways but there is often present a strong factor of psychic shock in addition, particularly amongst bombed civilians. Surgical shock and hæmorrhage are of course marked.

(2) *Recent cases.*—These have been under treatment for some hours or days and many of them are relatively clean. Others, however, may be very toxic and ill with gas gangrene and other infections, such as many of the cases evacuated from Dunkirk.

(3) *Re-operation cases.*—Most of these are recovering and do not concern us at the moment.

It can be stated at the outset that, in this type of work, it is considered that there is no place for such a toxic and damaging drug as chloroform. Ether is less severe in its effects on the organism but in view of its known deleterious action on the organs and tissues of the body and in the light of recent experience it is not considered justifiable to employ it when less toxic agents are available.

Experiences of the last war as reported by Marshall, support this view. The only claim that can be raised in favour of chloroform and ether is portability. What, however, could be more portable than a few ampoules of pentothal and a syringe? These will suffice in situations where portability is of paramount importance, and they are non-inflammable.

Marshall, Flagg and others showed clearly in the last war how deadly spinal analgesia can be in cases suffering from severe shock and hæmorrhage.

This leaves us with the gases, nitrous oxide and cyclopropane; and the barbiturates, pentothal and evipan.

Nitrous oxide is entirely without toxic effects on the body. When damage results from its administration, this is invariably due to oxygen lack. This has been convincingly demonstrated by C. B. Courville. Cyclopropane is almost as non-toxic (*vide* the work of Marshall and Daly, Eversole, Rowbotham, and many others), provided care is taken to avoid overdosage.

Shock is not a contra-indication to the administration of pentothal and evipan, properly administered, rather is the reverse outstandingly clear.

PREMEDICATION

Careful inquiry should be made as to how much and how recently morphine has been administered to the cases classed as immediate, and the degree of shock and hæmorrhage present should be estimated. Many of the patients need nothing. Omnopon gr. ⅓-⅔ and scopolamine gr. $\frac{1}{150}$ is adequate for the others.

TECHNIQUES

The patients can be roughly divided into extra-abdominal and abdominal cases. The former may again be divided into reasonably fit, toxic, shocked, and hæmorrhagic cases.

(1) *In reasonably fit patients.*—Pentothal 0·3-0·5 grm. (6-10 c.c. of the usual 5% solution) followed by gas and oxygen is almost invariably adequate for all extra-abdominal procedures. Very rarely a few hundred c.c. of cyclopropane "supplement" may need to be added, or perhaps a further small dose of pentothal.

(2) *In toxic cases.*—To avoid ether will be generally conceded to be most important. The same method as before can be employed and is far less likely to cause liver and other tissue damage.

In connexion with toxic patients it has been made abundantly clear by work on many gas-gangrenous patients (particularly those received from France last May and June) who were given large doses of "M & B", that there is no contra-indication to the administration of pentothal, even though the latter contains about 12% of sulphur.

It was reasoned that the sulphur being in firm combination with the barbiturate molecule would be unlikely to exert any deleterious effect, and such proved to be the case. No ill-effects whatever were observed on any one of a large number of cases receiving both drugs.

(3) *In shocked cases.*—Pentothal in divided doses, repeated as needed or given by continuous infusion by the method so admirably demonstrated by Rivett and Quayle has been found excellent, blood being substituted for saline when necessary. Nitrous oxide is not necessary and in fact is best omitted for reasons given in connexion with the next group. Oxygen from a Boyle's or similar machine, with plenty of re-breathing when necessary to produce stimulation with carbon dioxide, however, is very helpful.

(4) *In hæmorrhagic cases,* which will of course be shocked as well, two forms of tissue anoxia are likely to be present. *Anæmic* anoxia and *stagnant* anoxia. To administer an anæsthetic such as nitrous oxide, which is so weak as to be effective in many cases only in the presence of a considerably reduced oxygen percentage, does not seem to be a sound method in dealing with such patients. Pentothal, however, is a potent anæsthetic

and is excellently tolerated by them, especially if their oxygen-carrying handicap is overcome with oxygen and carbon dioxide as suggested before. A little of the anæsthetic it should be noted goes a long way in such circumstances as the following case will illustrate:

Illustrative Case No. I.—A soldier, aged 32. Exploration of wound for severe secondary hæmorrhage. Patient very pale and exsanguinated. No premedication was given. Induction was with 0·15 grm. (3 c.c.) of pentothal. This gave adequate anæsthesia for fifteen minutes. Two further injections of 0·15 and 0·1 grm. respectively allowed of the comfortable completion of the operation, which occupied in all, 45 minutes.

(5) With regard to *abdominal cases*: adequate relaxation can be obtained with a pentothal induction followed by cyclopropane. The following illustrative case will show the value of this technique in desperate cases.

Illustrative Case No. II.—A soldier, aged 30. Perforating gunshot wound of the abdomen 36 hours ago, no treatment yet. Acute peritonitis present. Collapsed, dehydrated, subnormal temperature, rapid and feeble pulse. Comatose and apparently moribund. Immediate laparotomy was performed under cyclopropane. Four intestinal perforations of small gut were found and sutured. The abdomen was drained. This patient's post-operative condition was excellent all things considered, but he only improved up to a point, and was opened up again 30 days later for drainage of pelvic abscess. He was still a very sick man. The same anæsthetic was given. After this operation he finally made a perfect and complete recovery.

These methods do not apply only to general surgery, but can be adapted to many special cases. A full description is beyond the scope of a short paper, but the example of adaptation to brain and skull wounds may be cited. Here success was attained by cocainization of the larynx, followed by induction with a small dose of pentothal. An intratracheal tube well lubricated with 10% percaine ointment was then passed and maintenance achieved with gas and oxygen, supplemented if necessary with occasional short-time additions of cyclopropane, at 50 - 100 c.c. per minute. This amount given with open circuit anæsthesia is insufficient to have any effect on bleeding, and can be stopped ten minutes before diathermy is to be used.

The difference in post-operative condition between the etherized and the non-etherized patients has been amazing and as a matter of clinical experience is far more impressive than any statistics. It has been noted by house surgeons and ward sisters alike, who are observing the patients closely all the time. Furthermore, a number of personal communications has been received from other observers adopting the same principles of avoidance of chloroform and ether which unreservedly confirms this fact.

Statistics are not easy to get together under wartime conditions, as a perusal of the literature of the last war indicates, but the table (p. 40) gives the results in 200 consecutive and unselected military casualties, anæsthetized by various anæsthetists, from amongst those dealt with at the time of "Dunkirk". A large proportion of these men had gas gangrene, and all were severely exhausted. They are divided simply into two classes, according to whether they were moderately or severely ill, and it should be noted that the grading was done in every case by the anæsthetist who administered the anæsthetic.

While it is not suggested that the deaths were necessarily anæsthetic deaths, the point is stressed that when patients die in the early post-operative period, the anæsthetic substances employed must be considered to have played a vital part in the result and may well have just tipped the scales. Therefore deaths occurring within seven days of operation have been taken as being germane to the point at issue.

The details of the two deaths were as follows:

I.—A soldier, aged 20. Suffering from severe gas gangrene of the whole of the left arm. He was very ill and severely toxic. The limb was amputated through the shoulder, under evipan followed by a long gas-oxygen-ether anæsthesia, accompanied by transfusion. He died 7 hours afterwards without regaining consciousness.

II.—A soldier, aged 36. Suffering from gunshot wound causing compound fracture of the humerus. Condition appeared to be quite good. The anæsthetic was gas-oxygen-ether. He died from pneumonia within seven days.

In direct contrast here are two further illustrative cases:

Illustrative Case No. III.—A soldier, aged 24. He was suffering from severe gas gangrene of the thigh extending right up into the buttock. He was very toxic and had a high temperature. The anæsthetic was pentothal induction followed by gas and oxygen. He made a perfect and uninterrupted recovery.

Illustrative Case No. IV.—A female, aged 24. Rescued from debris of a big building. She was desperately severely shocked and amongst other injuries was exsanguinated

from loss of blood from a pulped arm. Four hours resuscitation and four pints of blood were needed before she could be taken to the theatre. The anæsthetic was continuous pentothal through transfusion tube, amounting to 0·85 grm., and the operation time was about 40 minutes. No trouble was experienced and recovery from the operation was excellent.

200 MILITARY CASUALTIES.

"MODERATE"—154 CASES

Non-ether

	No. cases	Survived	Died 7 days	% mortality
*Barbiturate–N_2O–O_2 ..	80	80	0	0
N_2O–O_2	3	3	0	0
C_3H_6..	1	1	0	0
Total	84	84	0	0

Etherized

*Barbiturate–N_2O–O_2–E ..	51	51	0	0
N_2O–O_2–E	19	19	0	0
Total	70	70	0	0

"SEVERE"—46 CASES

Non-ether

	No. cases	Survived	Died 7 days	% mortality
*Barbiturate–N_2O–O_2 ..	31	31	0	0
N_2O–O_2	–	–	–	–
C_3H_6..	4	4	0	0
Total	35	35	0	0

Etherized

*Barbiturate–N_2O–O_2–E ..	4	3	1	25%
N_2O–O_2–E	7	6	1	14%
Total	11	9	2	18%

*Barbiturate signifies either pentothal or evipan—in most cases the former.

CONCLUSIONS

From the foregoing the following conclusions have been drawn:

(1) Nitrous-oxide-oxygen anæsthesia, preceded by a small induction dose of pentothal gives all the relaxation and quiet the surgeon needs for extra-abdominal work. Ether is not necessary, besides being a needless addition to the patient's burden.

(2) Cyclopropane, combined with a pentothal induction is effective for abdominal work.

(3) These anæsthetic agents are the least damaging and toxic at our command.

(4) The difference between non-toxic and toxic anæsthetic agents administered to patients already severely damaged frequently means the difference, quite literally, between life and death in the early post-operative period.

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[Dr. Mallinson demonstrated a new By-pass for a To-and-Fro Absorber, *see also Brit. M. J.*, 1940 (i), 774; 1941 (i), 17.]

Section of Neurology

President—GEOFFREY JEFFERSON, M.S.

[*March* 19, 1941]

DISCUSSION ON FAT EMBOLISM AND THE BRAIN

Dr. A. H. T. Robb-Smith : Fat embolism may be described as a condition in which there is fat circulating in the blood-stream in globules large enough to occlude the capillaries and induce multiple anoxæmic foci. It was first produced experimentally by Richard Lower in the seventeenth century, and the first adequate description of the clinical and pathological features was given by Wagner in the middle of the last century, but pathologists must be blamed for the widely accepted attitude that it is a rather uncommon complication of a fracture of a long bone. The condition has been more generally recognized in America and on the Continent than here, and this can probably be attributed to the fact that their organization for the investigation of violent deaths is much superior to our own. There is no doubt that gross trauma is the most frequent causative factor in fat embolism. In my series of 115 accident cases I regarded it as playing a significant part in the fatal outcome in 25%, and Vance, in a rather larger series, put the figure at 20%. Clearly the assessment of the importance of fat embolism in an accidental death is a difficult and arbitrary matter—in a man with a fractured base and gross cerebral laceration dying in a few hours it is immaterial how much fat embolism is present, whereas in a case of fractured tibia dying in three days with pulmonary or cerebral symptoms, the presence of fat embolism is probably significant.

Naturally the extent of the trauma is important; it is most frequent in cases of multiple fracture, particularly in those involving the long bones, but it may occur in cases in which the skull alone has been fractured, or indeed where there has been no fracture at all. I have looked for fat emboli in a large number of cases dying after cranial exploratory operations, and also in a smaller series of orthopædic cases where purposeful trauma has been applied to the bones, and have only found it in minimal degrees.

Apart from cases of accidental trauma, fat embolism may be found in severe burns (though it is usually slight in amount), following manipulations, or the therapeutic injection of oily solutions; and it appears to be an important and frequent complication of poisoning by ammonia and other alkalies. Although there may be a considerable lipæmia in diabetes, subacute Bright's disease and to some extent after an adequate meal, yet symptoms of fat embolism do not develop, as the emulsion is a very fine one.

There is still considerable disagreement with regard to the source of the fatty material and its mode of entry into the circulation. Rarely the injury may rupture a large vein and damage the surrounding fatty tissue so that a considerable mass of fat is drawn into the circulation but the mechanism is usually more subtle than that. Owing to the recognized association of the condition with fractures it has been suggested that fat from the marrow is forced into veins of the medullary cavity at the moment of impact, or that there is a slow seepage either by vein or lymphatic, of the extracellular fat that is found around a fracture, or that, as a consequence of the injury, substances enter the blood-stream and change the physical state of the plasma lipoids or lipo-proteins. The history of many but not all cases favours a local rather than a hæmic origin of the emboli. With regard to the traumatic cases arising without fracture, similar explanations have been put forward, and it has been shown that fat embolism can be induced in animals

either by local trauma or by centrifugalization. In alkali poisoning there is a considerable alteration in blood chemistry but whether a true hyperlipæmia is induced or a lipoproteolysis is by no means clear.

The clinical picture of fat embolism differs according to whether almost all the fat is held up in the lungs, or whether it enters the systemic circulation to produce emboli in the brain, heart, &c.

In pulmonary fat embolism it may rarely happen that a considerable mass of fat enters the circulation owing to the tearing of a large vein, and obstructs the pulmonary arteries or their main branches. In these cases the symptomatology is exactly comparable with a pulmonary embolism induced by a dislodged blood-clot.

The classical picture of pulmonary fat embolism is to be seen in an accidental injury usually with a fracture and often in cases in which there has been delay in immobilization. At first the patient may show symptoms of shock, but these pass off as the result of treatment, and the clinical condition appears satisfactory for a period ranging from a few hours to a day or so. There will then be complaint of vague pains in the limbs, a sense of thoracic constriction, and dyspnœa with a pale cyanosis; there is considerable distress, the pulse and temperature rise as well as the respiration rate but the blood-pressure does not fall. Examination of the chest reveals a few râles but no signs of consolidation, and the patient may bring up a little frothy sputum similar to that seen in acute pulmonary

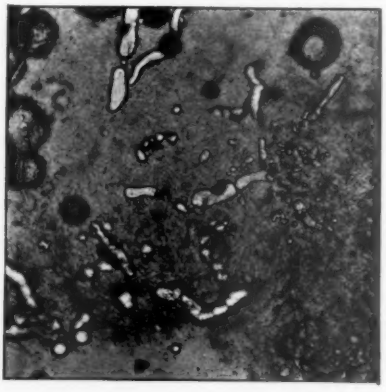

FIG. 1.—Pulmonary fat embolism. Fresh preparation of lung cleared with 2% potassium hydroxide. × 67.

œdema. There is no gross venous engorgement, but venipuncture is easily achieved in contrast to the difficulty often experienced in obtaining blood samples from the collapsed veins in shock. The patient may die during this anoxæmic phase with signs of acute right heart failure, but usually the severe symptoms diminish, the respiration rate continues high, sputum at first blood-stained and later purulent is brought up and signs of pneumonia develop which may resolve after about a week or end fatally.

The differential diagnosis in the acute anoxæmic phase is clearly between shock and internal hæmorrhage, and I have stressed the features distinctive of fat embolism which are essentially those of acute pulmonary œdema. In the later pneumonic stage a true pneumonic consolidation does develop with, in some cases, a secondary infection.

Skiagrams of the chest have been obtained in a few of our cases and in published accounts, and, though they show irregular opacities, yet the appearances are not characteristic enough to be of value, though the rapidity with which the opacities disappear is striking. Examination of the sputum in the acute phase is of no value but in the pneumonic phase fat will be found in considerable amounts; however, the interpretation of this is not easy for in many cases of chronic bronchitis much fat is brought up in the sputum and it is essential to differentiate between extracellular fat in large globules

and the histiocytes containing finely divided fat. It has been claimed that there is a sudden anæmia in cases of pulmonary fat embolism, but this has not been our experience.

The morphological lesions found at post-mortem are characteristic. The right heart is dilated, and on centrifugalization of specimens of blood from the right and left heart cavities it will be found that a considerable layer of fat forms on that from the right side but little if any on that from the left, though the arterial blood is much more concentrated. The lungs are heavy and show a mottled appearance owing to alternate areas of emphysema, œdema and congestion; fat may be seen, naked eye, on the cut surface, and a fresh preparation made by taking a small snippet of lung and clearing it for a few minutes in a drop or two of 2% potash readily reveals emboli (fig. 1). In sections embedded in paraffin all that can be seen is the congestion, œdema, and emphysema, but frozen sections stained for fat show the presence of large numbers of emboli (figs. 2 and 3). In the pneumonic phase the lung has the appearance to the naked eye and microscopically of a low-grade pneumonia, but frozen sections reveal much fat both in capillaries and in the alveoli; in the late pneumonic stages very little fat may be found in the lung although there are considerable amounts in the brain and other organs.

Symptoms of systemic fat emboli may follow those of pulmonary fat embolism but in a number of instances the pulmonary symptoms are trivial and the nosograph is essentially that of cerebral embolism. It has been suggested that in those cases which show cerebral symptoms without previous pulmonary ones the fat has passed through a patent foramen

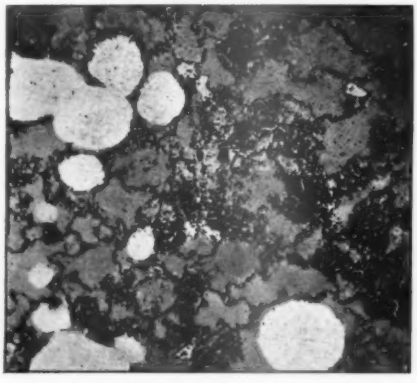

FIG. 2.—Pulmonary fat embolism. Showing zones of emphysema, œdema and interalveolar hæmorrhage. H. and E. × 67.

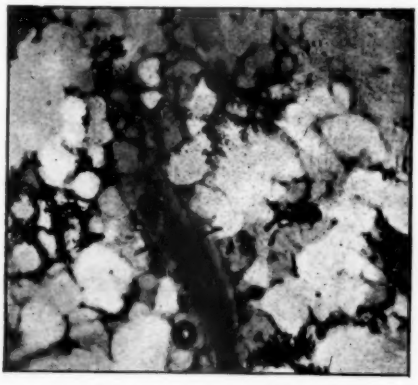

FIG. 3.—Pulmonary fat embolism. Frozen section showing emboli, congestion and emphysema. Osmic acid. × 22.

ovale, but this seems unlikely. In systemic fat embolism the symptoms do not usually develop until two to three days after the accident, and are characterized at first by a delirium which is frequently very violent, alternating with stupor which merges into coma; localizing signs are usually absent or, if present, are chaotic; hyperpyrexia is usual and it is not uncommon to find petechial hæmorrhages on the skin of neck, chest and arms, and their presence greatly facilitates a diagnosis.

Lumbar puncture shows no increase in intracranial pressure and no constant cytological or chemical change although fat has been described in the cerebrospinal fluid. Naturally in cases in which there has been a cerebral injury in addition, the picture may be obscure. Examination of the optic fundi may be of assistance, and Dr. Jameson Evans has recently described the ophthalmoscopic appearances in a patient with cerebral fat embolism who recovered. He was a man aged 23, who suffered fractures of several long bones, and three days after the accident he developed a surly subcoma and petechial hæmorrhages. Lumbar puncture gave a clear fluid under normal pressure but fat was present in the urine. Examination of the fundi revealed diffuse œdema of the retina, most marked on the macular side; there were also areas of crescentic pallor and subhyaloid hæmorrhages.

Eight days after the accident his mental condition began to improve, and at the end of a fortnight the eye condition was resolving. Another feature which has been described is segmentation of the columns of red cells in the vessels by the fat.

With regard to examination of the urine and blood for fat there is considerable disagreement. Blood fats from the point of view of the physical state have not been studied at all and if the urinary fat is to be examined certain precautions must be taken. The fat floats on the surface of the urine in the bladder and accordingly it is imperative that the bladder must be completely emptied, preferably by means of a catheter, which, needless to say, must not have been lubricated with oil. The urine should then be centrifugalized in a Babcock tube such as is used for estimating the fat content of milk.

At post-mortem the kidneys show no naked-eye changes but frozen sections show much fat in the glomeruli and indeed fat emboli may be found in all the viscera. A form of cardiac fat embolism has been described with cardiac irregularities, and in some cases with signs of coronary ischæmia, but I have not observed it although miliary foci of necrosis in the heart muscle are often found in systemic fat embolism.

Some observations on treatment.—The prophylactic treatment is the basic first-aid treatment of a fracture—as complete immobilization as possible. It is further recommended that manipulations should be carried out with a tourniquet in position and that this be released slowly. It has been shown in animals that a much larger amount of fat can be tolerated without symptoms if it is injected slowly. It has been suggested that effusions around fractures should be drained, but this seems of doubtful expediency, though it is true that fat embolism is much less frequent in compound than simple fractures.

In the stage of pulmonary œdema and anoxæmia, oxygen through a B.L.B. mask should be administered and, in view of Dr. George Graham's observations on acute pulmonary œdema, subcutaneous adrenaline should be tried: intravenous administrations of fluid should be withheld or suspended for they can only increase the pulmonary œdema, and indeed phlebotomy would appear rational and has been advocated. However, it is difficult to decide as to intravenous therapy in cases suffering from shock or blood loss which need either plasma or whole blood, yet from practical experience I am confident that only harm and sometimes a fatal outcome may result if this form of therapy is persisted in when signs of pulmonary œdema develop. The patients are more comfortable propped up. Morphia is probably best withheld and it is doubtful if either atropine or stimulants of the coramine type are of any value.

With regard to specific therapy numerous drugs have been proposed. Wegelin suggested the intravenous infusion of sodium carbonate to saponify the fat, but this is unsound theoretically and has not proved of value in practice. Recently Rapport has advocated the use of sodium desoxycholate intravenously in order to emulsify the fat and reduce the blood viscosity. We tried it on one patient and the pulmonary symptoms certainly improved but he developed cerebral fat embolism and died. In collaboration with Professor Burn we have been trying out its effect on animals with experimental fat embolism and so far it would appear to be definitely harmful. In the pneumonic phase symptomatic treatment must be followed and in cerebral fat embolism a similar course can only be suggested though repeated lumbar puncture has been advocated.

Prognosis.—In the past only the most severe cases have been recognized and the vast majority of these have ended fatally. Yet there is little doubt that in its severe and milder forms fat embolism is a more frequent complication of injuries, and it is probable that a more general recognition of the nosographs of pulmonary and systemic fat embolism will cause a decrease in the incidence of delayed shock, traumatic pneumonia and delirium tremens and an increase in the number of recovered cases of fat embolism and possibly a more rational form of therapy.

[Figs. 1, 2 and 3 are reproduced by courtesy of the *Lancet*.]

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Mr. Alan H. Hunt: The significance of fat embolism is undetermined. A few will overestimate its importance and, conscious of the frequency of its occurrence, will suggest it on every possible occasion; others will dismiss it as a problem hardly worthy of practical recognition. Its place in a consideration of the complications of trauma lies between these two extremes.

Traumatic fat embolism may be defined as the lodgment of numerous fat globules in the smaller vessels of the tissues. If we recognize that emboli of fat can be demonstrated in about 50% of the lungs of all cases that come to necropsy (Lehman and McNattin, 1928) and in about 85% of the cases of trauma (Lehman and McNattin, 1928, Vance, 1931), then we must have criteria of severity in order to be able to see the condition in its right perspective. Vance considers that severe cases are those in which fatty emboli can easily be found post mortem in the systemic as well as in the pulmonary circulation of the body. Dr. Robb-Smith (1941) has suggested a rough standard for counting the number of emboli in the lungs. A combination of these two methods provides us, as pathologists, with an estimate of the extent of embolism. Clinically we can only judge its incidence by the symptoms, signs and secondary effects. In fatal cases we can only tell the extent to which it contributed to the death of the patient by a careful correlation of the clinical and the pathological findings. In death following severe fractures fat embolism appears to occur in a severe form in at least 15% of cases, and to be the major factor in the fatal outcome in at least 5%.

That, in itself, should warrant its recognition by every doctor. It is one of the most important factors in any consideration of the differential diagnosis, prophylaxis and treatment of the complications of trauma. If an effective specific remedy for fat embolism is discovered, its routine prophylactic administration will have to be considered in a high proportion of cases of severe injury, whether fractures are present or not.

The pulmonary manifestations of the disease are essentially non-specific in nature, except in those cases in which the acuteness of the œdema appears to produce a critical anoxæmia. The patient may be almost normal until about two hours before death, when he suddenly collapses with a so-called "acute traumatic pulmonary œdema" which venesection fails to relieve. Microscopical examination of the lungs in such cases will show overwhelming numbers of fatty emboli within the smaller vessels. These emboli must have been accumulating for many hours during the symptom-free interval and the number that pass on to the body generally will vary.

The clinical manifestations of systemic or cerebral fat embolism are, in contrast to those of the pulmonary type, most characteristic. The multiplicity and changeability of the cerebral signs and symptoms, the cutaneous petechial hæmorrhagic rash, evidence of pulmonary œdema or pneumonia, the temperature, pulse and respirations chart, and possibly the discovery of fat in a catheter specimen of urine, constitute a typical syndrome. It is not common and it is a very serious disease. It seems to be exceptional for such cases to recover. Benestad (1911) reported three from Germany and Whitaker (1939) two from America.

Case report.—R. M., a healthy man aged 29, was knocked off his bicycle by the trailer of a lorry at 7.30 a.m. on March 9, 1939. He was completely aware of the accident and had no retrograde amnesia. The wheels went over his right shoulder and leg.

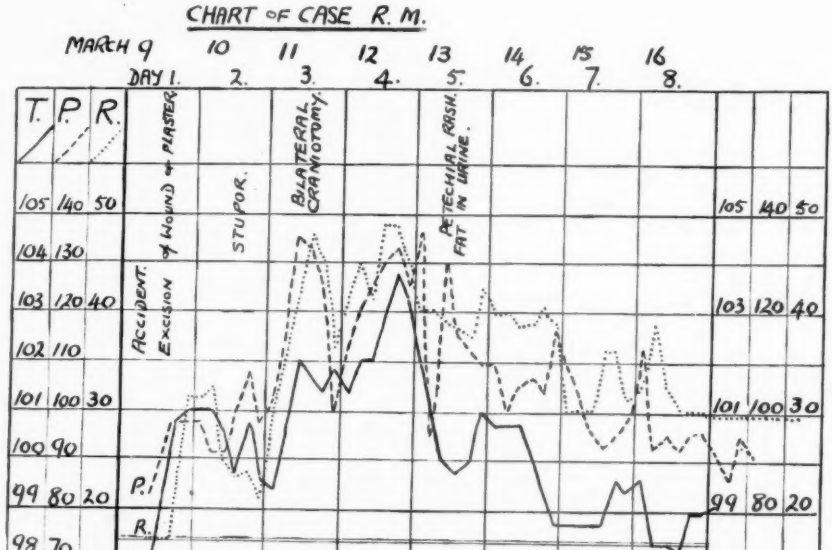
He was taken to St. Bartholomew's Hospital immediately and admitted under the care of Professor Paterson Ross, to whom I am indebted for permission to publish this case. The patient was shocked, but perfectly rational in his actions and speech. There was no evidence of an intracranial lesion. He had sustained a comminuted fracture of the right scapula, fractures of two right ribs (6 and 7), an open transverse fracture of the right tibia just below the middle of the bone, and fissure fractures of the right maxilla and squamous temporal bone. There were also present a small pneumothorax and some surgical emphysema of the chest wall, both on the right side.

The patient was resuscitated by general measures, the wound of the tibial fracture was excised under gas, oxygen and ether anæsthesia and a plaster applied. The right arm was put in a sling.

On March 10 the patient complained of pain in the chest on respiration. A change in his mental state was first noticed at 3.30 p.m. (32½ hours after the accident) when he could not be roused for tea. He became incontinent of urine and progressively more stuporous: he developed weakness of the right side of the face, and of the right arm and leg. Lumbar puncture revealed normal cerebrospinal fluid at a pressure of 180 mm. C.S.F.

On March 11 the temperature had risen to 102° F., pulse to 130 and respirations to 45. His right pupil had become larger than the left, but it reacted well to light. 100 c.c. of 50% sucrose injected intravenously produced no effect. The diagnosis of systemic fat embolism had been considered, but an acute subdural hæmorrhage could not be excluded. A bilateral exploratory craniotomy was therefore performed, but nothing abnormal was discovered.

On March 12 the temperature rose to 103·6° F. The patient could occasionally be roused and would sometimes take fluids by mouth He kept moving his left arm and leg in an entirely inconsequential manner, but the tendon reflexes were equal on the two sides. There was no sputum, no fat in the urine and no petechial rash. The blood-pressure was 120/80.



On March 13 the mental condition was unchanged. The state of coma varied but the patient could not be roused enough to speak. The characteristic minute petechial hæmorrhages of systemic fat embolism had appeared in profusion on the neck and over the shoulders, and in fewer numbers over the chest, abdomen, thighs, and arms. A catheter specimen of urine contained fat. The retinal vessels showed no fatty emboli or other abnormality. An X-ray of the chest showed no change in the pneumothorax, but there was some consolidation of the left lower lobe. The sputum contained encapsulated pneumococci, so sulphapyridine was administered.

March 14: Condition unchanged.

March 15: The patient was still very restless but considerably improved. He began to swear at all and sundry, thereby showing a certain interest in his surroundings. The hemiparesis had disappeared, the temperature had dropped to 99° F., pulse to 94 and respirations to 30.

The improvement continued. The temperature and respiration rate had settled to normal by March 18 (nine days after the accident), and the rash had disappeared by the 21st. He was then beginning to show some control of his sphincters and had become much more co-operative, though still liable to spells of drowsiness or delirium. The pulse became normal on the 23rd. Convalescence was interrupted by an attack of pleurisy lasting four days in the fourth week, when an X-ray of the lung fields showed that the consolidation of the left base had entirely resolved. Mental recovery was complete within a month from the accident.

He was discharged on April 17 and continued treatment as an out-patient till he returned to full work as a riveter in November 1939. Physical disability accounted for this delay. His mental condition was normal.

Now, in March 1941, he has only two complaints referable to his cerebral disease. He sleeps very little, so that he can do duty as an air-raid warden in Central London at night as well as a twelve-hour working day; and he complains of headaches when he rests. He describes the pain as nagging. It lasts about half an hour and occurs about twice in the twenty-four hours. I saw him last week and his intelligence is of a high order. His senses are normal, his mind is alert, his memory is excellent, he has a quick wit and he says he has became a voracious reader since he has been able to manage with so little sleep.

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Dr. Dorothy Russell: Within recent months two cases of cerebral fat embolism have come to necropsy at the Radcliffe Infirmary, Oxford. Both clinically and pathologically they serve to illustrate the main features of this condition which, as Dr. Robb-Smith has demonstrated, is far commoner than has been generally realized.

Case I. Clinical.—Male, aged 26 years (R.I. 10167). Fracture of left femur in motor accident. Admitted to hospital two hours later in state of profound shock with vomiting. Blood-pressure 86/36, temperature 99, respiration rate 30. Improved after receiving oxygen, 2 pints of plasma and radiant heat. Blood-pressure 105/75 six hours after accident. Half an hour later: pains and cramps all over, especially in chest and groins; restless, cyanosed and sweating; B.P. 120/75, pulse-rate 50. Cyanosis improved with administration of oxygen but otherwise condition unchanged. Twelve hours after accident: respiration rate 44; crepitations and moist sounds in chest. Pulmonary fat embolism diagnosed. Treatment with sodium desoxycholate begun (for details of this case *see* Robb-Smith, *Lancet*, 1941, p. 138); condition improved. Day after accident leg set up in extension with tibial pin. Two days after accident: respiration rate 25 to 32; coughing up blood-stained sputum; mentally confused, stupor alternating with violent irritability; no evidence of increased intracranial pressure. Restlessness relieved with nembutal but general condition steadily deteriorated with rising temperature, pulse and respiration rate, and signs of consolidation in lungs. Death followed six days after the accident.

At necropsy the lungs showed gross fat embolism in the pneumonic stage.

Brain.—Macroscopic: The cerebral hemispheres were somewhat soft, particularly the lateral surface of the left occipital lobe. The cut surfaces showed irregular diffuse pinkish areas of hyperæmia distributed throughout the cortex, subcortical white matter and basal ganglia, the intervening areas being pale and moist (fig. 1). Petechial hæmorrhages were numerous in the engorged areas of the cortex and often formed small groups; they were less numerous in the subcortical white matter. A conspicuous group, about 1 cm. in diameter, occupied the left side of the corpus callosum. There was gross softening of the cortex and white matter forming the lateral border of the left occipital lobe. No macroscopic changes were present in the brain-stem and cerebellum.

Microscopic: In all areas examined a variable number of the cortical capillaries, and more rarely the precapillary arterioles, were occluded by rounded or oblong masses of fat (fig. 2). In addition a large number of capillaries appeared to be blocked by fibrin thrombi while others were distended with collections of neutrophil leucocytes. In many instances there was no evidence of parenchymal change in the immediate

neighbourhood of the blocked vessels. Elsewhere, however, both the fat emboli and fibrin thrombi were associated with small hæmorrhages or with areas of anæmic necrosis. These changes were not as a rule sharply defined: gradations in the degenerative changes in bodies of neurones could be traced between complete necrosis at the centre

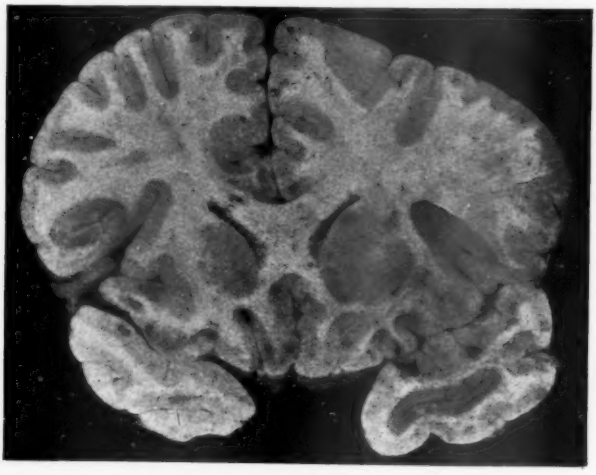

FIG. 1.—Coronal section of brain showing patches of hyperæmia and petechial hæmorrhages.

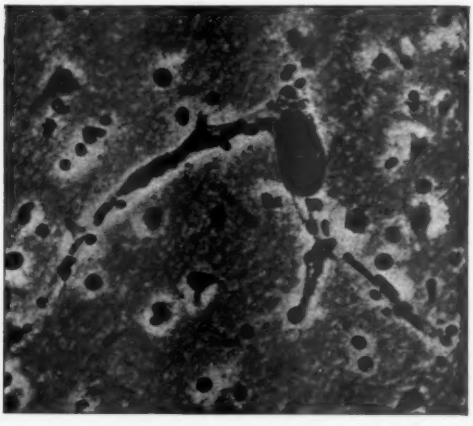

FIG. 2.—Cortical capillary occluded by fat embolus. No softening or hæmorrhage in adjacent tissue. Silver carbonate and Sudan III. ×210.

of the focus and the well-preserved cell bodies in the surrounding cortex. Within the area axis cylinders had undergone fragmentation and variable numbers of amœboid microglial cells had assembled. In the subcortical white matter both hæmorrhages and anæmic necroses were scarcer and more sharply defined. As in the cortex they were

FIG. 3.—Ring hæmorrhages in corpus callosum. Loyez' hæmatoxylin. × 21.

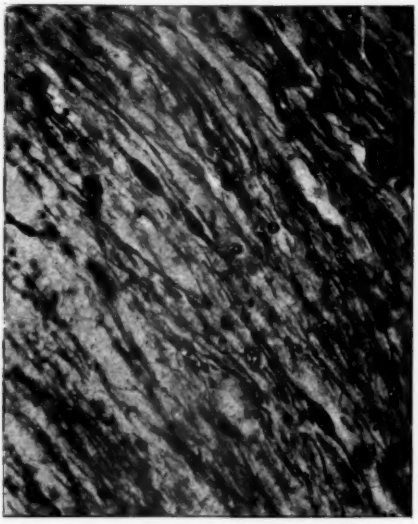

FIG. 4.—Bulbous swellings and retraction-balls on axis cylinders at margin of ring hæmorrhage. Silver carbonate for neurofibrils. × 250.

FIG. 5.—Occlusion by thrombus of meningeal artery over occipital lobe in Case I. Weigert's iron hæmatoxylin and van Gieson. × 15.

associated with fibrin thrombi in some instances, with fat emboli in others. The hæmorrhages tended to be of ring form and showed the characteristic necrosis with loss of myelin in a central area surrounded by a zone of red corpuscles in which axis cylinders were fragmented and bore retraction-balls (figs. 3, 4).

The area of softening in the occipital lobe proved to be an extensive anæmic infarct due to obliteration by thrombus of a large meningeal artery (fig. 5). One end of the thrombus showed early organization. The presence of fat in this thrombus could not be established since the tissue had been embedded in paraffin. Frozen sections of an adjacent block showed no changes in the meningeal vessels, nor did these vessels in other parts of the cerebrum show occlusion of their lumina by either fat or fibrin. The evidence therefore is insufficient to show whether this thrombus was embolic or formed in situ.

A moderate number of fat emboli were found in the *basal ganglia* and in all layers of the *cerebellar cortex;* few were present in the white matter

The *choroid plexuses* showed conspicuous blocking of capillaries and small arterioles either by fat or fibrin (fig. 6). Elsewhere the vessels were greatly engorged and some-

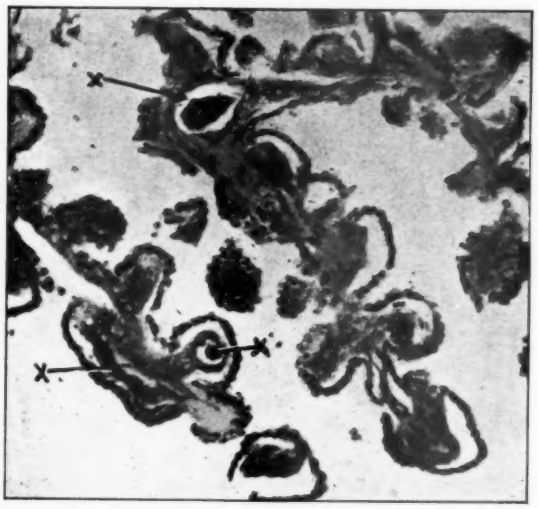

FIG. 6.—Choroid plexus showing occlusion by fat of several vessels in stroma (x). Silver carbonate and Sudan III. × 110.

times distended by masses of leucocytes. The degree of vascular disturbance was greater here than in any other part of the brain examined. The epithelium of the plexuses had undergone severe degeneration of an albuminous character often leading to necrosis. A large proportion of the nuclei were pyknotic. This degeneration, though patchy, appeared to involve the greater part of the epithelium.

Case II. Clinical.—Male, aged 22 years (Military Hospital for Head Injuries, No. 131). He received a depressed fracture of the right frontal bone, fracture-dislocation of the right ankle, together with bruising of both groins, in a motor-cycle accident. When admitted to hospital an hour later he was conscious but confused and irrational, being disorientated in space and time. He was suffering from shock. The head wound was dressed with proflavine and his condition improved after receiving 3 pints of blood plasma. The ankle was then manipulated and set in plaster. Soon after this he became pale, the respiration rate increased and it was found that blood was being lost from the scalp wound. Accordingly this was redressed, a portion of the depressed bone being removed, the scalp stitched and a firm dressing applied. Two pints of blood were given by drip transfusion and, on the day following the accident, he had improved. The

head wound was then opened up, the loose fragments of bone removed and the exposed tissues dusted with sulphathiazole. His condition after this was satisfactory until the following day when he became restless, the pulse-rate increased and he began having epileptic fits at intervals of from fifteen to thirty minutes. In these the eyeballs turned upwards, the pupils being moderately dilated and fixed to light. After holding his breath for thirty seconds there was twitching of the lower jaw. His respiration became stertorous; pulse-rate 100. Lumbar puncture yielded slightly blood-stained fluid containing 40 mgm. of protein %, 3 lymphocytes and 36,848 red cells. He died on the following day, that is, three days after the accident.

At necropsy the lungs showed evidence of fat embolism; there was gross tearing and bruising of the adductor muscles of both thighs. The scalp wound was healthy.

Brain.—Macroscopic: At the site of injury in the right frontal lobe there was an oval area of superficial laceration, measuring 5 by 2·5 cm., accompanied by softening and diffuse hæmorrhage extending into the brain substance as a wedge up to 2·5 cm. in depth. This area occupied a parasagittal position immediately posterior to the frontal pole. There was slight œdema of the whole of the anterior half of the lobe. Apart from this there was nothing of note in the cut surfaces except for a few punctiform hæmorrhages in the left superior frontal convolution and in the left inferior temporal and hippocampal convolutions.

Microscopic: Examination of the lacerated area in the right frontal lobe showed no noteworthy features beyond the degeneration, fragmentation and hæmorrhage consequent upon trauma. Elsewhere the cerebral cortex, subcortical white matter and the choroid plexuses showed vascular and parenchymal changes similar to those already described, but much sparser. The cerebellum, including the dentate nucleus, was not affected.

DISCUSSION

The clinical and pathological features in Case I may be regarded as classical. The sequence of events after the accident was sufficiently clear-cut to enable a clinical diagnosis of cerebral fat embolism to be made. In Case II, on the other hand, it is hardly surprising that this diagnosis was missed in view of the coincidence of a severe brain injury, and the frequency with which epileptiform attacks may occur in the first days after cortical injury. The possibility of cerebral fat embolism as a complication of head injury should always be borne in mind when injuries have also been inflicted upon other parts of the body.

The histological features of the two brains examined agree substantially with the detailed descriptions published by Gauss (1916) and Neubürger (1925). Neither of these authors, however, mentions the choroid plexuses. My experience suggests that these structures are extensively involved in cerebral fat embolism, which is perhaps not surprising in view of their highly vascular character and their function in the formation of the cerebrospinal fluid. The observations in these human cases agree with those of Fazekas (1935, 1938) in experimental fat embolism produced by sodium hydroxide and ammonium hydroxide poisoning in cats and guinea-pigs. In these experiments the choroid plexuses were more extensively involved than any other tissues after the lungs. Investigation might show that embolism of the plexuses is reflected in alterations of a characteristic kind in the cerebrospinal fluid.

I wish to thank members of the Staff of the Radcliffe Infirmary and of the Military Hospital for Head Injuries for the use of their Medical Research Council records.

ADDENDUM

Since these notes were written a second case has been observed in which cerebral fat embolism complicated a depressed fracture of the right frontal bone.

This patient, a male, aged 39 (Military Hospital for Head Injuries, No. 581), was admitted eight hours after injury in a motor-cycle accident. Apart from the head injury he had slight abrasions of the right leg and a fracture of the right clavicle. He was suffering from shock and was conscious but not confused. Blood-pressure 130/75 mm.; pulse-rate 58. Treatment on the day of admission was confined to excision of the scalp wound and reduction of the fractured clavicle. Following this he became drowsy, cyanosed and apathetic; moist sounds were found in the chest accompanied by cough. Three days after the accident his temperature had risen to 103° F.; there was neck rigidity and a bilateral Kernig's sign. Diminished movement of the lungs at both bases and

a respiration rate of 40 raised the problem whether pneumonia or meningitis was mainly responsible for his condition. Repeated lumbar puncture had consistently yielded blood-stained fluid containing an excess of white cells, but no organisms were found in films or cultures. In view of the involvement of the right frontal sinus in the fracture it was decided to explore this region: the depressed fragments of bone were removed, softened brain beneath these was sucked out and the area packed with sulphanilamide powder. Nevertheless the general condition of the patient steadily deteriorated with maintenance of pyrexia, high respiration and pulse rate and he died nine days after the accident.

At necropsy the lungs showed bronchopneumonia and scanty fat emboli. There was no evidence of infective meningitis; slight subarachnoid hæmorrhage involved the greater part of the brain. On section the brain showed a blotchy hyperæmia and some petechial hæmorrhages as in Case I. Microscopically fat emboli were rather sparse in the cerebrum and affected the white rather than the grey matter; they were more numerous in the cerebellum and were abundant in the choroid plexuses. There was no evidence of infective meningitis. Traumatic softening was localized to the right frontal pole.

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Dr. J. G. Greenfield: The brain with fat embolism which I examined was that of a man of 35, wounded on October 20, 1940, by an anti-aircraft shell that fell on the ground a few feet away from him. He sustained a compound fracture of the right foot and puncture wounds in the middle of the right thigh and on the right iliac crest. There was also a superficial wound over the left iliac fossa. He was taken to St. Mary's Hospital, Plaistow, where it was noted that his pupils were dilated, the left being larger than the right, and that he was practically unconscious. The right leg was amputated and the abdominal wound excised and sutured. He was transferred next day to Claybury Emergency Hospital. He was there noted to be drowsy with some twitching of the face and hands. There was a gross general increase of tone in the limbs, and examination of the right arm started clonic spasms of the right face, arm and leg, spreading to the left side. The plantar reflex on the left side was extensor in type. He died on October 23, three days after being wounded.

Post-mortem examination revealed small hæmorrhagic areas in the lungs and numerous petechial hæmorrhages in the white matter of the cerebrum. After fixation the right cerebral hemisphere was sent to me for examination. It showed small brownish streaks in the white matter of the frontal lobe, some small hæmorrhagic areas in the frontal cortex and a larger but very limited hæmorrhage into the splenium of the corpus callosum.

On microscopical examination of frozen sections, stained by Scharlach R and hæmatoxylin, many vessels both in the cortex and white matter were found to be plugged with fat, which was partially anisotropic. The number of vessels affected varied from one place to another; in some areas of the cortex almost every vessel was filled with fat, other areas showed none.

In the white matter there were in addition very numerous small perivascular areas of demyelination, extending a variable distance from the wall of a small vessel which was usually seen to be plugged with either fat or thrombus. The largest of these areas measured 600 μ in transverse diameter, the smallest about 100 μ. They were often oval, suggesting that they followed the vessel along its course, but no vessels were cut in a sufficiently longitudinal direction to be sure of this point. The tissue in most of these zones could not be called necrotic, since there was little alteration of nuclei; the myelin however failed to stain either by Scharlach R or by Weil's iron-alum hæmatoxylin method, although no breakdown products of myelin could be seen with Scharlach R. The axis cylinders were present in the demyelinated area but showed evidences of degeneration such as swellings and irregularities on their course.

The margin of some of these areas was fairly sharply defined; in others there was a more gradual transition towards healthy myelin, through a zone in which the myelin sheaths were beaded and stained poorly. In some of the areas there was a central

zone of necrosis, measuring about a half or two-thirds of the diameter of the demyelinated area, and usually surrounded by an irregular circle of microglial cells. A similar central zone of necrosis ringed by microglial cells was present in some perivascular hæmorrhages, which showed the typical picture of ring hæmorrhage. But no hæmorrhage was present in the great majority of the areas. The macroscopical appearances gave, in fact, no hint of the large number of these small areas visible in sections stained for myelin. They were especially numerous in the occipital lobe.

Some of the areas in the outer zones of the white matter passed for a certain distance into the cortex, and here, in addition to loss of myelin, there was great shrinkage and loss of staining power of the neurones. The neuroglial and microglial elements appeared to be little affected in these areas, and the walls of the vessels showed little change except proliferation and swelling of the endothelium in some. Other areas appeared to be confined to the outer part of the cortex. These also showed shrinkage and loss of staining of neurones, and in some no neurones were demonstrable. Here as in the white matter the axis cylinders were relatively little affected. The demarcation of these cortical areas was remarkably sharp. One passed immediately from an area in which the neurones were scarcely recognizable to one in which they showed no appreciable damage.

These well-defined areas of destruction of neurones and myelin are quite unlike those seen in any other condition. While those in the white matter resembled in size the perivascular areas of demyelination in the encephalitis which may follow variola, vaccinia, measles, influenza, &c., there is in this condition a great proliferation of microglia throughout the demyelinated zone, even in cases dying a very few days after the onset of cerebral symptoms; and they do not show the smaller central area of necrosis ringed by a single layer of microglial cells, nor the cortical areas of neuronal degeneration. These appearances should therefore make it possible to recognize fat necrosis by ordinary tissue stains even in non-hæmorrhagic cases.

This case shows that hæmorrhagic lesions may be insignificant in brains with fat embolism, and certainly much less prominent than in most fatal cases of cerebral contusion. And although petechial hæmorrhages in the white matter are the chief or the only abnormalities apparent on macroscopical examination of the brain in fat embolism, it is evident that ischæmic degeneration of neurones and myelin are of much more importance in the production of symptoms.

Dr. A. C. Frazer desired to ask one or two questions of Dr. Robb-Smith. After every fatty meal quite a large amount of fat passed into the blood-stream. It was almost certain that some sort of fat embolism actually occurred and the capillaries became blocked with fat. A large amount of fat also got caught up in the lung. What, in Dr. Robb-Smith's opinion, was the relationship of the intake of food to the pathological factor? Accident cases were obviously more likely to have a high blood-fat content than cases coming to autopsy in the ordinary way. Although the accident might have occurred some time after the taking of food, the condition of shock would tend to delay the dispersal of fat in the capillaries, and therefore one might expect to find fat remaining in those vessels. It would be interesting to know what was the state of nourishment in the cases described.

The second point concerned the relationship with anæsthesia. In a number of stages of blood-fat, the dispersal of the fat and its presence in certain organs, particularly the liver, were quite definitely affected by anæsthesia.

Thirdly, had Dr. Robb-Smith any information about the protein of the blood in these cases? It had been recently shown that the protein was the most fundamental stabilizing factor for blood-fat.

Dr. A. Meyer said that in collaboration with Dr. Nightingale, he investigated a psychotic case, in which cerebral fat embolism was caused during treatment with triazol (*Journal of Mental Science*, 1940, 86, 819). Besides fat emboli in the cerebrum and cerebellum and areas of necrosis there was a widespread thrombosis of large and medium sized blood-vessels. At the time of writing the paper Dr. Nightingale and he were of the opinion that the thrombosis might have been caused by severe disturbances of the blood circulation following fat embolism. This was in accordance with the views expressed by Neubuerger and Weimann. There was some doubt, however, whether this interpretation was correct. Whatever the explanation might be, it was interesting that Dr. Russell also found thrombosis in one of her cases of cerebral fat embolism.

How difficult the interpretation of the lesions may occasionally be was further shown by a case of cerebral fat embolism which was recently observed among a series of air-raid casualties investigated at the Central Pathological Laboratory by Professor Nevin

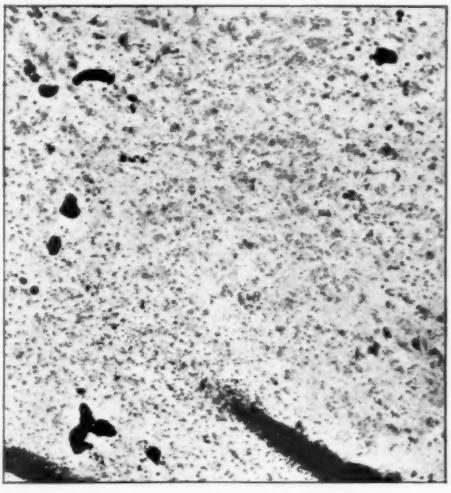

FIG. 1.—Typical fat emboli in the brain (scharlach R stain).

FIG. 2.—Occipital lobe with the characteristic elongated areas of necrosis (Heidenhain's stain for myelin).

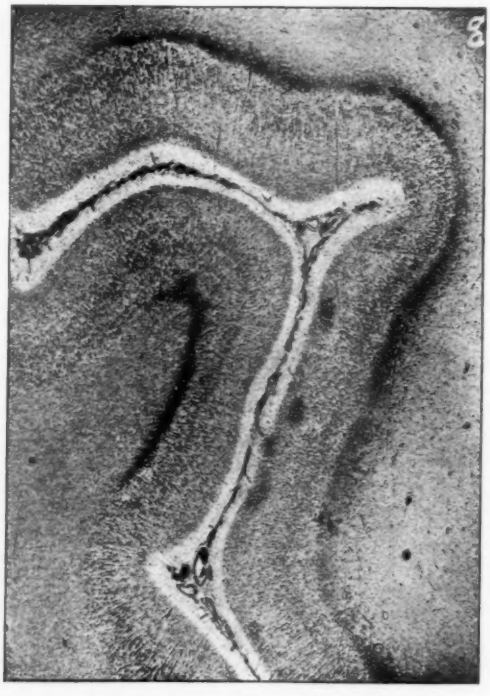

FIG. 3.—The same as fig. 2 (Nissl's stain).

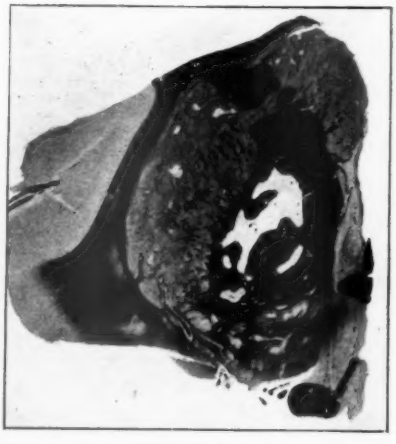

FIG. 4.—Selective softening of the globus pallidus (Heidenhain's stain for myelin).

and himself. This was the case of a child who had been in a bomb explosion, sustaining fracture of skull and superficial injuries of the skin. The child died within a week of the injury. When a post-mortem examination was made fat embolism of the lung was found. The brain showed superficial bruises which were probably the sequel of mechanical injury. In addition, histological examination showed numerous fat emboli in most parts of the brain including the cerebellum (fig. 1). There were many areas of necrosis and early softening which had an unusual appearance in that they stretched for considerable distances along the borderline of the cerebral cortex and white matter, involving the deeper layers of the cortex and the adjacent superficial white matter. This was particularly marked in the occipital lobe but occurred also in many other parts of the cortex (figs. 2 and 3). This " quasi " systemic appearance of softening had been observed by different workers in various conditions of a vascular pathology. For the sake of comparison he showed the same appearance in a case of carbon-monoxide poisoning of his own observation. This case died sixteen years after the acute poisoning and many glial scars were found of the same localization.

The most surprising finding in the brain of the child was a bilateral selective softening of the globus pallidus (fig. 4). It was interesting that while an abundance of fat emboli was seen in many parts of the brain so far not a single one was found in or near this softened zone of the globus pallidus.

In considering the pathogenesis of this case one possibility was that fat embolism was the result of the skull fracture and that at the same time carbon-monoxide poisoning occurred owing to the emission of gases following the bomb explosion or other circumstances. The clinical history gave no clue in this direction. On the other hand none of the changes was absolutely specific to carbon-monoxide poisoning. Selective softening of the globus pallidus had been described in a great variety of other conditions of anoxia. Rotter had found it in a case of head injury with ensuing respiratory failure. Dr. Robb-Smith had pointed out the importance of secondary anoxia in fat embolism. So far selective softening of the globus pallidus had not been seen in cases of uncomplicated cerebral fat embolism.

Both cases indicated that while cerebral fat embolism may undoubtedly lead to severe necrosis and hæmorrhage there may be complications which may account for at least a part of the lesions. This point is particularly important in regard to air-raid casualties in which among others carbon-monoxide poisoning is always a possibility.

Dr. H. C. Stewart said that concerning the origin of this fat there were two main probabilities. Either the fat came from the food or else from the depôts and especially from the parts of the body in which the tissues had been damaged. Had Dr. Robb-Smith made observations on the temperature of the limb or other part that had been damaged? Again, after death did the section of that part show any alteration in the consistency of the fat? In other words, was it more fluid than fat in the rest of the body? In their physiological studies these fat particles were very difficult to break down, and he felt that the changes necessary to produce coagulation or confluence of fat particles big enough to block these vessels would have to be very profound. It seemed to him therefore that the fat probably came from the damaged part itself.

Mr. A. Dickson Wright recalled a case of a woman on whom he had operated for a bone graft. After three days her respiration rate increased, she became very ill, went into a coma and died on the seventh day; post-mortem examination revealed fat embolism. Since then he had always felt that the reservoir of fat within the bones was potentially dangerous and that, if it is exposed at operation, the wound should be well flushed out with ether, in order to get rid of any free fat globules. He remembered many years ago reading a paper by a Japanese author who had evolved a technique for estimating the size of fat globules in the blood-plasma. If, after a fracture, he found globules of such a size as were likely to produce the condition of fat embolism, he watched carefully for the development of symptoms. He wondered whether Dr. Robb-Smith had ever encountered this paper: the method might be of value when a method of treatment of this condition is evolved.

Major D. E. Denny-Brown asked if it was known how long the myelin changes took to develop. He remembered being very surprised on studying Scharlach sections of the brain from a case of fat embolism shown him some two years ago by Mr. Hunt to

find that, although the cerebral vessels were frequently filled with fat, there was no myelin degeneration. Death had occurred after about thirty-six hours. The importance of this point was in relation to the supposed pathology of states of unconsciousness due to trauma in the absence of gross cerebral lesions. Great significance had been attributed to multiple petechial hæmorrhages in the brain. But generalized petechial hæmorrhages throughout the hemispheres were very rare; for example, five cases were reported by Cassassa (1924) out of thousands of autopsies on cases dying as a result of head injury. If these generalized petechial hæmorrhages were related to states of traumatic unconsciousness and confusion, the pathology of the condition was not only rare but also quite possibly only that of early cerebral fat embolism, before change in the myelin had occurred. Martland and Beling (1929) stated that out of Cassassa's five cases one certainly had fat emboli, and also one case of multiple petechial hæmorrhages reported by Osnato and Giliberti (1927).

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OSNATO, M., and GILIBERTI, V. (1927), *ibid.*, **18**, 181.

Dr. Eric Gardner said there was one aspect of this problem which had a considerable practical importance. It concerned those cases in which death was far too common after road accidents, and the following instance might be taken as a type.

A young man was run down by a lorry, and his leg was crushed from the knee to the ankle. Although he was not severely shocked on admission to hospital and was sitting up on his stretcher smoking and talking, it was deemed advisable to wait for some four hours before attending to his leg. He was kept warm during this time and was given morphia. Under an anæsthetic of gas and oxygen the leg was examined, and although there was little hope of saving it, it was thought inadvisable to amputate, and it was put up for the time being in a moulded plaster gutter, which necessitated a good deal of manipulation. He never fully recovered consciousness and died some six hours later. Subsequent examination showed a most extensive degree of pulmonary fat embolism; fat being found not only in the capillaries of the lung but blocking many of the larger vessels.

It is possible that an early amputation might have saved this boy's life, but in all such cases, as the danger of fat embolism came to be realized, so too would the necessity for extreme gentleness in manipulating this type of fracture.

He did not think that pulmonary fat embolism was a common complication of fracture in young people, unless as in the case quoted above, the injury was unduly severe. It was possible that in young people the heart was able to clear the lung, and this might explain why cerebral fat embolism appeared to be more common in them than in the old. It was noteworthy that all the instances of cerebral fat embolism mentioned during the course of this discussion had occurred in those under 30, and that tallied with his experience.

In old people, on the other hand, pulmonary complications were exceedingly common after an injury such as a fracture of the neck of the femur, when the fat was probably derived more from the bruised tissue than from the broken bone. Many of these old people died from hypostatic pneumonia within a week of their injury, but examination invariably showed extensive fat embolism blocking the pulmonary capillaries and slowing the circulation, but it was unusual to find any degree of fat in the cerebral vessels in such cases.

He also referred to those cases, admittedly not common but still too frequent, where death occurred during the remanipulation of a fracture under an anæsthetic. The surgeon was often inclined to doubt the pathologist's finding of fat embolism, maintaining that he had carried out many such procedures without ill-effect. But sudden death did occur under these circumstances, sometimes even in cases where two or three previous manipulations had been performed safely. Here again extreme gentleness in these operations was indicated.

The President said that one of the points which appeared to be dominant in all contributions (in the literature as well as in the papers just read) was that in order to obtain fat embolism most surely the bone must be injured. That was significant. The surgeon at his operations was accustomed to interfere considerably with body fat. In doing

gastric operations or colectomies on fat people, for example, he handled, pulled, or squeezed omentum. In amputating the breast he manipulated fat. It might be that the method he adopted in doing so, whereby he ligatured all the vessels, had an important preventive effect. But there may be a second explanation which left the first one untouched, namely, that it was the type of fat which was different, or if not that, or in addition to that, the vessels might be different in the medulla of the long bones from what they were in the other tissues he had mentioned. There was no doubt that the intra-osseous veins—the veins of the medulla—were different from the types of veins met with in the abdominal cavity and the subcutaneous tissues. They were not veins in the ordinary sense of the word, and it might be quite possible that there was a forcing back of fat into the vessels of the medullary cavity after a manner which did not occur in other regions. He himself first heard about this question of fat embolism thirty years ago. Sir Rickman Godlee and Gwynne Williams published a paper (*Lancet*, 1911 (i), 1062). Amongst the cases discussed in that paper there were two of fat embolism of the brain, proved at post-mortem. One of them, as in the case that Dr. Hunt had just described, was operated on as a probable cerebral hæmorrhage, and it must be admitted that there were times when it was extremely difficult to know whether a head injury had occurred at the same time as the accident and whether the symptoms were due to an intracranial hæmorrhage. In both cases there were coma, restlessness, delirium, and so forth, but of course the picture was really not the same on close analysis. There was the lowered blood-pressure, the greater cyanosis, and quite a number of points that impressed the experienced clinician and showed him that the case was really not a head injury. Yet, it was a source of possible confusion.

In this connexion, American writers in particular had raised the question of the type of anæsthetic used—not just the anæsthesia but its type—and it was interesting to note that in this paper by Godlee and Gwynne Williams chloroform was used and not fat-solvent ether.

Some experimental workers had wondered whether the thrombosis which occasionally accompanied a fracture of the lower limb might be due to fat embolism. They had observed in experimental animals a tendency to endothelial proliferation in the vessels of the limb. It was indeed a pity that the opportunities for examination were becoming more and more limited to coroner's cases, so that in the end we are likely to have what has already happened in America, namely, the accident side completely divorced from the general treatment in the hospital.

Dr. Robb-Smith (in reply to Dr. Frazer) said that with regard to the degree of nourishment, it had been maintained that obese people were more liable to develop fat embolism than thin people, but in his series of cases he had considered the weights of the cases, and these were not significant. As for the sort of meals they had been having just before the accident, he had not investigated this, nor had he any idea as to the temperature of the limb that was exposed to the injury.

So far as he had gone with dark-ground illumination the character of the fat globules of a physiological lipæmia were far smaller than the globules one saw in fat embolism; the difference was enormous. Further, as he had mentioned, if one examined the tissue around a fracture one would find post mortem—and he believed at operation as well—liquid fat lying there, and that fat was present in very large globules. It was quite clearly extracellular, partly marrow fat and partly connective tissue fat. The cell membrane ruptured and the fat was released. He was strongly in favour of the view that the fat was derived from the traumatized area, but in some cases, as in the case of poisoning, the evidence was not so good. Dr. Macfarlane and he were investigating the possible presence of lipo-proteinase in the blood of people suffering from trauma, but this work was still in the very early stage.

As for anæsthesia, the vast majority of the cases he had examined did not have anæsthetics, or only gas and oxygen. But there was experimental evidence that in animals, where fat embolism had been induced by injection of fat and the animal killed while under ether anæsthesia, the degree of embolism was much less than in a controlled series. On the other hand, if one waited for the animal to regain consciousness and for the ether to be dispersed, then the actual degree of embolism was much more marked than in the control series. It had been suggested that it was a good thing for accident cases to be given ether anæsthesia, not so much for ease of manipulation, but just as a prophylactic measure. The evidence, as far as it went, was that it was a bad thing, not a good thing.

On Dr. Gardner's point, he had seen cases develop massive fat emboli following manipulation, and in quite a number of cases of re-manipulation one found fat in the urine occurring a short while afterwards, some twenty-four hours or so. It had been suggested that in cases in which there was a danger of fat embolism it would be useful to cannulate and drain the part, wash through with some fluid and close up.

He agreed with Dr. Gardner that cerebral fat embolism appeared in young people; but as the vast majority of severe traumata occurred in young people he did not know how significant it was.

He emphasized the point which Dr. Hunt had raised, that one must not go away with the idea that fat embolism was the most frequent complication of trauma. There was always a danger of popularizing a condition and giving it undue prominence. An example of this at present was the attention paid to blast, which was regarded as the common cause of death among the victims of an enemy bomb. Probably one would find that fat embolism was a frequent complication of trauma, but that it was not all-important.

Section of Orthopædics

President—S. L. Higgs, F.R.C.S.

[*April* 26, 1941]

Meeting Held at the Wingfield-Morris Orthopædic Hospital, Oxford

A Report on Cases of Septic Arthritis

By W. B. Foley, F.R.C.S.

Mr. W. B. Foley reported a small series of 15 cases of acute septic arthritis treated in the Wingfield-Morris Orthopædic Hospital during the past eight years. These cases were all primary blood-borne infection of the joints concerned; cases secondary to osteomyelitis of bone, and local infections from without by penetrating wound or injury were excluded. The chief interest of the series lay in the fact that the majority of these cases were treated by repeated aspiration without operative drainage of the joint. The beneficial effect of aspiration is probably due to two causes. It relieves tension inside the distended joint capsule with, very often, notable relief of pain, and it withdraws infected, bacteria-laden fluid from the joint, allowing secretion of fresh synovial fluid containing phagocytes and antibodies. The initial aspiration therefore was performed as soon as possible after the diagnosis had been made and was repeated during the first week or so as often as was deemed necessary in relation to the general and local condition. A general anæsthetic was usually necessary on each occasion, but intravenous pentothal, or gas and oxygen, was sufficient, and caused little distress or discomfort to the patient.

Immobilization of the affected joint was essential in every case. This was effected in the hip-joint cases by placing the patient on a Jones' abduction frame with traction to the affected limb, the patient being placed on the frame usually while under the anæsthetic given for the initial aspiration. In knee cases a Thomas knee splint with traction provided the best form of immobilization and free access to the joint. Other joints such as the elbow and ankle were best immobilized in plaster with a window for inspection and aspiration. Splintage was maintained until the patient had been apyrexial for several weeks. It was then either modified or discontinued and the patient left free in bed.

The range of passive movement was then tested at weekly intervals and if increasing the patient would be allowed up on crutches or fitted with a caliper in the hip cases and weight bearing only gradually resumed after a further interval of several months.

Mr. Foley said that he was not in favour of the practice of early movements of these joints during the acute inflammatory stage, and did not believe that prolonged immobilization prejudiced the ultimate return of mobility in the joint. In several of the cases

subsequently shown a very full range of movement had returned in spite of immobilization for as long as six or eight weeks.

Since their introduction drugs such as sulphapyridine, sulphathiazole and proseptasine, had been used as an adjunct to the local treatment and were of undoubted value. However, some of the best results in this series had been obtained in cases treated before these drugs were on the market. A lantern slide was then shown of the results in these 15 cases (*see* tables below) analysed in relation to the type of treatment. In nine cases the infecting organisms were the *Staphylococcus aureus* and in six cases *Streptococcus hæmolyticus*. In discussing the tables Mr. Foley pointed out that the poor results in the staphylococcus group had some explanation in the fact that the three cases resulting in ankylosis which were treated by aspiration and drainage were children whose initial treatment was carried out at other hospitals and in whom there had been a delay in starting treatment, in two cases of three weeks and in one of ten days. The fatal case was that of a boy of 5 who was gravely ill and was one of the early cases treated before the days of modern chemotherapy, and probably the severity of the toxæmia in this case would have produced the fatal result, whatever method of treatment had been adopted. The case of ankylosis treated by repeated aspiration was a disappointing one as this man had had staphylococcal osteomyelitis of the femur ten years previously and might have therefore been expected to have had a higher resistance to staphylococcal infection. Among the streptococcal group there were fewer cases of complete ankylosis but also a smaller percentage of cases which regained full movement. The X-rays also showed more damage to the joint surfaces in the streptococcal cases than in the staphylococcal.

STAPHYLOCOCCUS AUREUS INFECTIONS.

	Deaths	Ankylosis	Limited movement	Full movement	Total
Total cases	1	4	1	3	9
Repeated aspiration only	-	1	-	3	4
Aspiration + drainage or drainage only	1	3	1	-	5

Joints affected: Hip 7, ankle 1; knee 1.

STREPTOCOCCUS HÆMOLYTICUS INFECTIONS.

	Deaths	Ankylosis	Limited movement	Full movement	Total
Repeated aspiration only	-	1	3	2	6

Joints affected: Hip 3; hip + shoulder 1; hip + ankle 1; elbow 1.

Cases were then shown with radiographs and temperature charts. These included three staphylococcal joints which had recovered with full movement and two streptoccocal infections which had recovered with partial movement.

In conclusion Mr. Foley said that this series was too small for generalizations, but that he was convinced of the value of repeated aspiration and would continue to use it as a first line of treatment. It was a minor and non-shocking procedure, a consideration not without importance in dealing with infection of a major and deep-seated joint like the hip in a very ill and toxic patient. He had shown that it could be followed by a very complete restoration of function. At the same time if repeated aspiration appeared to be failing to control the general or local situation, one should be prepared to consider open drainage.

Although Mr. Foley's report on results of treatment was limited to cases of primary blood-stream infection of joints, he thought the method equally applicable to local infections by penetrating wound or to effusions which sometimes accompanied metaphysial osteomyelitis or preceded the appearance of a small, solitary, epiphysial bone focus. When a primary bone infection, however, frankly invaded the adjacent joint, the surgical drainage of the bone must usually be extended to the joint, and the prospect of recovery with movement was then very remote.

The Spread of Bacteria and Toxins from Infected Wounds; the Clinical Application of Laboratory Findings.—J. M. BARNES, M.B.

The following is a brief description of some experiments carried out by Dr. J. Trueta and myself on the spread of bacteria and toxins from the tissues.

Older writers had shown that bacteria injected under the skin could be grown both from the blood-stream and from the lymph glands draining the area within a very few minutes. They concluded that they only reach the blood by way of the lymphatics. We have confirmed this in the following way. Under anæsthesia the femoral vessels were isolated in the groins of rabbits, and under a dissecting microscope the main lymphatic trunks were destroyed; a stout ligature was then placed round the remaining tissues of the leg at this level, leaving the lower part of the leg connected to the body only by the femoral artery and vein. Deep wounds were then made into the muscles of the calf of the leg, and into them was dropped a saline suspension of bacteria. The limb was moved for a few minutes and ten and sixty minutes later blood was removed from the ear vein. At this time the animals were killed and the spleen removed. The blood samples and spleens were cultured. When bacteria were placed in wounds of normal animals the blood and spleen cultures were invariably positive. In our experimental animals they remained sterile. In other words bacteria failed to reach the blood from a limb whose lymphatic drainage had been destroyed.

We then investigated the absorption of certain snake-venoms. Using black tiger snake-venom we found that a dose given to an animal prepared in the way just described failed to kill it within sixty minutes. The same dose killed normal animals within seven minutes. Further experiments showed that whereas obstruction of the lymphatic return invariably delayed the death of the animals, obstruction of the venous return alone had no effect. We concluded therefore that this venom was absorbed by the lymphatics.

Since mechanical obstruction of the lymphatics is obviously not a practical procedure we decided to test the absorption from immobilized legs, since the lymph flow is known to be minimal under these conditions. Using smaller doses of venom that killed control animals within three hours we found that of 13 animals given the venom into a limb immobilized in plaster 4 survived, 4 lived for over twenty-four hours, and 5 survived for over eight hours. Using Russell viper venom in a small series of kittens we obtained similar results. On the other hand we found that cobra venom was absorbed at the same speed from normal and from immobilized limbs; it behaves in the same way as strychnine and other crystalloids which are known to be absorbed by the blood. The difference is probably due to the fact that the first two venoms possess large molecules, whereas the molecule of the cobra venom is small.

We then turned our attention to the bacterial toxins. Little is known about their chemical composition, but they are known to consist of large molecules similar in size to those of serum proteins. Twelve rabbits were given a dose of tetanus toxin into the leg; six remained free and six had had their leg immobilized in plaster prior to the injection. The control animals all died within five days with generalized tetanus; of the immobilized animals two only died of tetanus, and those nine and fourteen days after the injection.

In view of the obvious importance of the lymph in the carriage of toxins and bacteria we tried to find out more about the factors governing its flow from limbs. It has long been known that with a limb at rest no lymph will flow from a cannula tied into any of the main lymphatic trunks, but that it commences to flow as soon as the part is moved. We found that the maximum flow from the leg of an anæsthetized dog took place when active muscular contraction with full movement was brought about by stimulation of the nerves to the leg. If the limb was then enclosed in plaster and the muscular contractions continued the flow became very small. In other words, it is the movements and not the increased metabolic activity of the muscles that are mainly responsible for the flow of lymph.

Inflammation is also known to increase the flow of lymph, and we found that if the paw of a dog was inflamed by hot water the flow of lymph from a cannula in the lymphatics in the groin increased within about sixty minutes. We noticed that this increase coincided with the development of œdema, and it has been shown experimentally that in inflammatory œdema the lymphatics, far from being occluded, are held widely open. This was clearly shown by the fact that pressure on the œdematous foot produced a copious flow from the groin as long as pressure was maintained.

We then tried the effect of preventing œdema by enclosing the foot in plaster as soon as it had been scalded, and in this case the flow never increased to the same extent as in the leg where the foot remained free. Nevertheless there was still some flow in spite of the partial immobilization, but we found we could still further reduce this if local drainage was provided by incisions into the foot after scalding and before enclosure into plaster.

ABSTRACT

The Spread of Bacteria and Toxins from Infected Wounds; The Clinical Application of Laboratory Findings.—J. C. SCOTT, M.S., F.R.C.S.

From the clinical point of view, observations on cases treated by the closed plaster technique have led to the conclusion that the following conditions, presented in order of importance, are chiefly concerned with maintaining consistently satisfactory results and avoiding complications:

(1) Adequate excision and drainage of the wound.

(2) Adequate immobilization.

(3) Careful selection of the time for changing the first plaster and careful avoidance of unnecessary movement of the limb when the plaster is changed.

(4) If the above conditions are observed, the bacterial flora is on the whole of little significance. The complete investigation of bacterial flora present under the plaster has been carried out in a limited number of cases.

Fat Embolism.—A. H. T. ROBB-SMITH, M.D., and J. C. SCOTT, M.S., F.R.C.S.

Dr. ROBB-SMITH's part in this paper is included in his contribution to the Discussion on Fat Embolism and the Brain held by the Section of Neurology (*v.* p. 639).

Mr. J. C. SCOTT showed a case and described two others in connexion with this paper.

Section of Dermatology

President—Major W. J. O'Donovan, R.A.M.C.

[*May* 15, 1941]

An Unusual Example of Lupus Erythematosus.—Godfrey Bamber, M.D.

Mrs. M. D., aged 29, was first seen on 31.12.40, when she complained of large patches on the legs that had first appeared four years ago and had returned every winter. In summer the areas became much less conspicuous but did not disappear entirely.

Examination showed large reddish-purple slightly scaly areas on the lower halves of the legs with smaller patches below the knees. On the sides and soles of the feet there was the same discoloration without scaling. The legs were cold to the touch, but there was no conspicuous follicular cyanotic stippling as in erythrocyanosis. On the backs of the hands and wrists were small dull red macules and small areas of atrophy on the backs of the fingers. The patient said that the lesions on the hands ran a course similar to but milder than the patches on the legs.

I think that these persistent polymorphic erythematous patches with a seasonal exacerbation come into the category of Hutchinson's chilblain lupus, but not into the lupus pernio-sarcoid group. Even in the larger plaques neither tumefaction nor dense infiltration was a feature.

The patient has now had injections of bismuth oxychloride and in spite of the persisting inclemency of the weather the discoloration has faded more rapidly than before, although the patches are still perceptibly colder than the surrounding skin.

Melanoderma of Face, Neck and Forearms of Unknown Origin.—F. W. Jacobson, M.D., and H. Ucko, M.D.

In August 1940 Mrs. A. J., aged 47, developed acute redness and irritation on both forearms and neck. She was treated by her doctor with a black lotion and with ointments. After disappearance of the rash a brown-blackish discoloration appeared at the previously affected areas.

Since February 1940 Mrs. J. has been employed at sewing army and police uniforms. She works along with 25 other women, none of whom developed a rash. She has never suffered from skin diseases before and has not taken arsenic or other drugs known to produce melanosis.

No previous history of venereal disease or of any apparent endocrine disorder. Mrs. J. stopped menstruating in September 1939. Until then, her periods had always been regular and normal. No complaints of menopausal disturbances. No evidence of deficient diet leading to avitaminosis. Family history does not reveal abnormalities of pigmentation.

On examination.—Forehead, face, anterior part of neck, both aspects of arms and back of hands show a diffuse dark discoloration of the skin with a peculiar violet hue, especially

on the face. On both sides of the neck between lower jaw and sternomastoid muscle the pigmentation forms a network similar to that seen in poikilodermia of Civatte. There is a slight atrophy of the skin with a mild degree of lichenification on both forearms.

General examination.—Slight but definite protrusion of the right eyeball but no signs of thyrotoxicosis. Pulse-rate 75, blood-pressure 130/85. Liver and spleen not enlarged. Skiagram of chest: Nothing abnormal. Urine normal.

Blood-count: R.B.C. 5,250,000; Hb. 90%; W.B.C. normal. Differential cell count: Basos. 1%; eosinos. 1%; neutros. 66%; lymphos. 30%; monos. 2%. Blood-sugar (fasting) 85 mgm. %.

Gynæcological examination (Mr. A. Davis).—Nothing abnormal.

Conclusion.—The patient has developed, in consequence of a probably acute dermatitis, a melanosis of the previously affected parts. Whether this was due to a photosensitization of unknown origin (? handling of dyed fabrics) is impossible to say. All the known and described exogenous (Hoffmann-Habermann) and endogenous (Riehl) causes for the development of a melanosis do not apply to this patient.

Discussion.—Dr. F. PARKES WEBER: I think this is an atypical case of chloasma uterinum. The menopause is sufficient to give rise to chloasma uterinum in special constitutions and I think that in certain individuals various kinds of war work may act as predisposing causes. It is perhaps not the exact kind of war work, but rather the whole alteration of the life which acts on a patient. I have seen a somewhat similar case (that of a woman ambulance driver, aged 35) recently. There was no obvious uterine or ovarian cause (the patient had prevented herself from having children), but I believe that one should not say that pigmentation is necessarily not chloasma uterinum because there is no actual uterine or ovarian disease. In that particular lady I think the excitement of war work and certain family troubles, some associated with the war, had acted as predisposing causes of the chloasma uterinum.

Dr. A. C. ROXBURGH: One cannot regard this as a case of chloasma because there is a definite atrophic change in the skin with a reticular arrangement, especially on the sides of the neck, whereas my idea of chloasma is that it is a purely pigmentary change and nothing else. I saw the case to which Dr. Parkes Weber has referred and I agreed with him that it was chloasma uterinum but in my opinion it was quite different from this one.

Dr. JACOBSON: In the 1940 Yearbook of Dermatology and Syphilology by Wise and Sulzberger (p. 304), a symposium of all the causes leading to melanoderma is given and one paramount cause is photo-sensitization.[1] It is possible that patients will become photo-sensitized by some endocrine influences, especially as we know that the pituitary gland secretes a melanophoric hormone. The literature states, and we know, that after exposure to sunlight acute dermatitis connected with a kind of melanoid hue sometimes arises that may be most persistent and incurable. I think it is possible that the fact that this woman lost her periods in comparatively early years, in addition to some other endocrine factor, may have given rise to her condition, but there must be some exogenous factor. I am going to do a patch test (with the fabric handled by the patient) and although I do not expect much result I should like to report to the Society later if the test is positive.

POSTSCRIPT (13.8.41).—Patch test: negative. Ophthalmological report (Mr. A. Sorsby): "Apart from distinctly unusual punctate opacities in the lens and right exophthalmos with some upward displacement, there is nothing to be found. ? a melanotic mass in orbit downwards. But this is a guess. I suppose it is a case for observation."

Histological Demonstration.—W. FREUDENTHAL, M.D.

(1) Nævus cells in sebaceous glands.

Dr. W. Freudenthal, whose talk was accompanied by slides, gave an account of some unusual histological sections, the first relating to the origin of the nævus cell. He said:

The first section is a small contribution to a much-discussed problem in dermato-histology—the origin of the nævus cell. More than forty years ago Unna expressed the view that nævus cells were of epidermal origin. They could sometimes be seen "dropping" from the epidermis in the form of cell nests.

Unna's theory has been opposed by Masson who found in nævi arrangements which resembled nervous tissue, especially nerve endings. He came to the conclusion that the

[1] Arias, Pessano and Radice, *Rev. argent. dermatosif.*, 1940, **24**, 117.

nævus mollis was essentially a tumour of nervous origin, viz. a neuroma of the tactile nerve endings. Masson denies that the cell nests seen "dropping" from the epidermis are derived from the basal cells, but thinks they are proliferations of Langerhans' cells. These he regards as cells of nervous origin, which as epidermal melanoblasts also play an important part in the formation of pigment.

Most observers agree with Masson's findings, even if they disagree with their interpretation. I myself have seen repeatedly nerve formations in nævi; they were particularly well developed in a case in which Dr. W. N. Goldsmith had assumed their presence beforehand on clinical grounds.

Fig. 1 belongs to a case which, clinically, was a pigmented hairy mole on the chin of a girl 8 years old. It showed no tendency to grow, but for cosmetic reasons Dr. J. H. Twiston Davies decided to remove it. The section is that of a typical nævus mollis with a fair amount of pigment in the uppermost part of the cutis and shows no signs of malignancy.

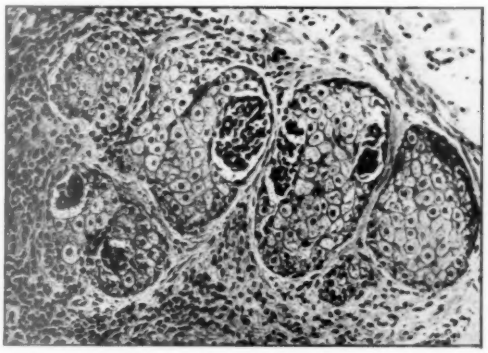

FIG. 1.—Nævus cells in sebaceous gland. × 140 (Dr. J. H. Twiston Davies' case).

A special feature, however, is that throughout the section in many of the sebaceous glands an aggregation of cells is seen which are very similar to those of the surrounding nævus cells. Being closely aggregated, these cell heaps look fairly dark, but no pigment is seen in them. Otherwise the sebaceous glands are normal; signs of inflammation are absent. The most likely explanation is that these cells are nævus cells which have arisen from the wall cells of the sebaceous glands. These wall cells are highly differentiated basal cells, which produce sebaceous cells. It has not been suggested that they can form pigment or that nerve cells or Langerhans' cells are found amongst them.

Although in such an intricate question as the origin of the nævus cell, the findings in a single lesion cannot be held to prove anything, yet they are in my view a point in favour of the epidermal theory. They are in accordance with Unna's [1, 2] findings of nævus cells arising from hair follicles and sweat ducts. A possible co-ordination of Unna's and Masson's theories is to regard the nævus mollis as the result of a disturbance in the early ectodermal layer.

(2) Connective tissue in syringoma cysts.

The second case is concerned with a small detail in syringoma, which had puzzled me once before; the present case may offer an explanation.

Dr. L. Forman who kindly allowed me to show the section, described the lesions clinically as small, soft, raised or slightly pedunculated tumours on the axillæ, groins and lower abdomen of a woman aged 26; they were said to have been present from childhood.

The biopsy, taken from the axilla, shows a typical syringoma with its numerous cysts and short tubules. An unusual feature is the presence of small fibrillary masses

staining red with van Gieson, found lying in some of the cysts. What were these masses? I could find no reference to them in the literature. Their size and structure made it unlikely that they were a secretion product. It seemed probable that they were connective tissue, but how could its presence be explained in cysts with an epithelial lining? One might think they were bits of connective tissue, which during sectioning had been pushed into the cysts, but by examining serial sections this could be excluded.

Finally, one place in the section seemed to offer an explanation. A fairly large cyst is divided in two by an epithelial septum which enclosed some red material, obviously connective tissue, showing a small central capillary. I should like to regard this as a bifurcation of a tubule. Later the epithelial septum perishes, leaves the more resistant connective tissue fibres behind to be found floating in the cyst.

REFERENCES

1 UNNA, P. G. (1894), " Die Histopathologie der Hautkrankheiten ", p. 1150. Berlin.
2 Id. (1910), " Histologischer Atlas zur Pathologie der Haut ", p. 116, figs. 116-118. Hamburg und Leipzig.

Sections of Otology and Laryngology

COMBINED ANNUAL MEETING

[*May* 2, 1941]

OTOLOGICAL SESSION

Chairman—LIONEL COLLEDGE, F.R.C.S.

(President of the Section of Otology)

DISCUSSION ON CHEMOTHERAPY, SEROTHERAPY AND HÆMOTHERAPY IN OTOLOGY AND LARYNGOLOGY

Colonel L. E. H. Whitby: In dealing more especially with the chemotherapeutic side of this discussion I must first emphasize that the principles for the use of sulphonamide drugs are the same in this region of the body as in any other. Firstly it is essential for the infecting organism to be sensitive to the drug employed, and because this region is so frequently infected with the β-hæmolytic streptococcus, which is sensitive to all three compounds in common use (sulphanilamide, sulphapyridine, sulphathiazole), there is great scope for use and for assessment. In general, acute infections always respond better than chronic ones and early stages are more amenable than late. In ear, nose and throat infections the important bacteria sensitive to sulphanilamide are β-hæmolytic streptococcus, meningococcus, *B. proteus, B. coli, B. pyocyaneus,* whilst those sensitive to sulphapyridine include all the foregoing as well as pneumococcus, *B. friedländer* and many strains of *Staphylococcus aureus.* Sulphathiazole has approximately the same range as sulphapyridine but is claimed to be more active against *Staphylococcus aureus* and *B. friedländer.* One may emphasize the enormous advantage of a bacteriological examination taken at the outset. This provides an explanation of failures and disappointments and is also a safeguard; a point which the Chairman (Colledge, 1941) has emphasized in a recent letter to the medical press.

The second principle is that the drug must reach an effective level and be maintained there until a full clinical result is obtained. If it takes longer than about seven days to achieve an obvious clinical result none can be expected with the drug being used though a change of preparation may produce the desired effect. An effective level is only maintained by regular four-hourly dosage and this means that the hours of night must not be omitted. As a corollary to this principle one may say that if a clinical effect has been obtained it is unwise to omit treatment entirely for a further forty-eight hours.

The third principle is to be sure that the drug is called upon to act in a favourable medium and position. These drugs are active in blood, in serum, in tissue fluid and in serous exudate, but are greatly inhibited, if not quite inactive, in a frankly purulent medium. Laudable pus is the province of surgery not of chemotherapy, the timely

combination of the two can achieve wonders. Infections in bone are usually little affected by sulphonamide drugs. There is much scope for clinical judgment in deciding what phase an inflammatory reaction has reached and what result is to be anticipated with either chemotherapy or surgery or both. There can never be any rule of thumb and indeed this is the same in all branches of medicine.

With these principles in mind one can now consider the expected effects of chemotherapy on an infection in the various regions of the ear, nose and throat.

First, with regard to acute otitis media and some of the grave complications—mastoiditis, sinus thrombosis, meningitis, septicæmia and cerebral abscess—which may follow. The statistical analyses of Bowers (1940), Horan and French (1940) and Fisher (1939) leave no doubt that the early and adequate administration of sulphonamide drugs

ACUTE OTITIS WITH AND WITHOUT CHEMOTHERAPY.

		No chemotherapy		With chemotherapy	
Authority	Period	Cases	Developed mastoid	Cases	Developed mastoid
Bowers	1937-40	180	24 (13·3%)	207	12 (5·8%)
Horan and French	1934-37	607	138 (22·7%)	—	—
Horan and French	1937-39	—	—	621	21 (3·4%)
Fisher	1938-39	95	66 (69%)	88	7 (8%)

markedly reduces the incidence of mastoid complication and the number of cases which progress to a point requiring paracentesis. It is significant that Horan and French had no deaths in a series of 621 cases of acute otitis media when combining chemotherapy with judicious surgery (*see* Table).

However, it does not necessarily follow that these good results are as rosy as they appear to be on the surface. Streptococcal and, to a less extent, pneumococcal disease of the upper respiratory tract is frequently secondary to influenza or one of the acute specific fevers, and it is in severe epidemics of these diseases when resistance is low and highly invasive strains of bacteria are widely distributed that the most troublesome cases of otitis are met with. There have been no such serious epidemics in the past few years and it is noteworthy that in another field of streptococcal disease, namely puerperal sepsis, it is considered that the virulence of the infecting strains has been of a lower order than in the previous decade.

To the extensive statistical analysis of numbers sufficient to allow of sound deductions, one can add the carefully studied smaller series of cases, such as the one recently published by Jessiman (1941), so that even allowing for variations in clinical material, circumstances and virulence, one may conclude that the evidence is unmistakable of the powerful effect of chemotherapy in acute ear disease. There is no doubt that the treatment must be handled boldly and with judgment, with an eye to possible risks. Each individual case requires consideration as to whether surgery is also required, which sulphonamide compound to use, and in what dose. I have always taken the view that if the middle ear on clinical probability appears to contain frank pus, paracentesis is necessary. This provides an opportunity for an exact and often rapid bacteriological diagnosis. Such a lesion is an abscess which requires drainage. The role of chemotherapy is then to prevent spread and to hasten healing. But if the lesion is at the stage of hyperæmia, acute congestion or sero-sanguineous exudate, recovery without drainage is possible and may be extremely rapid.

When conservative treatment is being used a most careful and frequent watch is necessary for the development of mastoid extension. At this time the temperature chart may be dangerously misleading. I have myself come to attach as much importance to the general well-being of the patient, discounting the depression, nausea or vomiting, which may be due to the drug itself. Those who are particularly anxious about the toxic effects of the drug should pay less attention to cyanosis, which is immaterial, than to the development of lassitude and weakness. If these appear prominent it is wise to examine the blood for evidence of agranulocytosis.

Whatever drug is used it must be given early and in full dose, and should be continued for some days after the disappearance of symptoms. Because the majority of cases are due to β-hæmolytic streptococcus, sulphanilamide offers a reasonable chance

of success for empirical treatment and has the advantage of causing less gastric disturbance than sulphapyridine. On the other hand, sulphapyridine offers a wider chance of success because it includes in its range the pneumococcus and many strains of staphylococcus; it is usually well tolerated by children. It remains to be seen whether more experience will show that sulphathiazole lives up to its reputation for non-toxicity and whether its potency for staphylococcus is as great as preliminary enthusiastic reports suggest.

As to exact dosage, there is no doubt that this should be the accepted full amount according to weight, that is an amount which is known to lead to and maintain a blood concentration of 10-15 mgm.%. For a quick effect the loading dose needs to be large. The following table provides a basis:

DOSAGE OF SULPHONAMIDE DRUGS IN ACUTE OTITIS MEDIA.

Weight	Loading dose (grm.)	Maintenance dose four-hourly (grm.)	Total dose first 24 hours (grm.)	Total dose 7 days (grm.)
10 st. or more	3	1	8	44
8-9 st.	2	1	7	43
7-8 st.	2	0·75	5·75	32·75
4-6 st.	1·5	0·5	4	22
2-3 st.	1·0	0·25	2·25	11·25

This table concerns oral administration which is always the route of choice. When the urgency of the condition or clinical state demands intravenous therapy the case is probably one in which mere conservative measures cannot be safely employed. While on the subject of dosage one cannot emphasize too strongly the futility and danger of prolonged and inadequate dosage which may sufficiently control the more obvious signs of serious complications, creating an atmosphere of confidence, and yet fail to control or eradicate the infective process completely. This toying with a powerful remedy is a common abuse of chemotherapy, and is dictated particularly by fear of agranulocytosis and other complications. Yet inadequate dosage demands a prolonged course and this in itself invites the very complications it is wished to avoid. Patients taking these drugs should be confined to bed.

As to duration of course, the case which does not recover on full doses within seven days almost invariably needs mastoid drainage. It is probable that failure to deal with the infection indicates bony involvement which, as in any other part of the body, is rarely controlled by chemotherapy.

One of the most satisfying results of chemotherapy is the way in which the sulphonamide drugs have altered the prognosis in meningitis of all types, whether they be primary or secondary to ear infection. When meningitis occurs there can be no question that drainage of the primary focus must be carried out. I have seen more than one case of pneumococcal meningitis where the meningeal infection has been treated as primary and temporarily controlled by one, two, and, sometimes, three courses of sulphapyridine but relapsed on cessation of the course. Only after the third relapse and too late to save life has the ear been examined to reveal a silent but obvious primary focus responsible for the constant reinfection of the meninges.

When one turns to chronic aural suppuration the results of chemotherapy have been disappointing. This again in my opinion is because the infection has involved bone. Nevertheless some of the more troublesome secondary organisms, such as *B. proteus* and *B. pyocyaneus*, can often be eliminated. Skin infections from the constant discharge can be greatly influenced by the local application of sulphanilamide with a moist saline dressing, having first cleaned up the skin surface with hypertonic saline.

With nasal sinusitis the reported results have been variable and on the whole disappointing. The anticipated effect would be such as is obtained in other cavities. When the mucosa is merely in a state of congestion a good result can be anticipated. When pus formation is advanced or bone becomes involved, then not much benefit can accrue.

As to tonsillitis and adenitis, there is a generally accepted clinical impression that when a sensitive organism is the infecting agent the course of the disease is shortened and the complications reduced. It is nevertheless difficult to be absolutely dogmatic

because it takes a vast number of most careful records to provide material for a statistical analysis when the criterion of judgment is the shortening of the period of disability in a disease which is rarely mortal. No one nowadays would, however, fail to prescribe sulphanilamide in an acute streptococcal tonsillar infection. Too early cessation leads to recrudescence. Tonsillar carriers of streptococci are not benefited. There has been much controversy as to whether sulphonamide alone or combined with antitoxin reduces the incidence of complications in scarlet fever. Thompson (1941) concludes that chemotherapy plus antitoxin gives the best results. Enterprising commercial firms have marketed sulphonamide sprays for local application to the pharynx. There is no evidence that these are effective, nor is benefit to be expected from the application of the drug to intact mucous membrane. Attack from within should certainly be more effective.

From the general aspect all are agreed that the results from these drugs vary from person to person. The complete understanding of these variations will take a long time; many of them cannot be controlled. It is quite certain that one strain of an organism may be more sensitive than another. Then there is the make-up of the individual and his general resistance, for the final elimination of the infection rests with the body and not with the drug. This is the great argument for the judicious combination of drug treatment with those antitoxic sera known to be potent and is an aspect which should never be neglected in dangerous cases. Then there is the vexed question of the variation in amount of acetylation: one person may acetylate and render inactive 75% of the drug administered, another only 10%. The relation of this phenomenon to activity, toxicity and for variation in dose has hardly passed the speculative stage.

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Dr. H. F. Brewer: The new chemotherapeutic agents have an action which is entirely antibacterial and they do not affect toxins other than by influencing the organisms producing them. Appropriate antitoxic sera are still of value, if only as adjuvants to chemotherapy; also, supplementing chemotherapy with a suitable antibacterial serum may enhance the effect.

In considering serum therapy certain basic principles still hold good even in its present limited use. The first is specificity (both for species of organism and type), the second, potency, and the third, early administration; closely related are optimal route and adequate dosage, whilst the final is the importance of accessory treatment—e.g. adequate surgical drainage of any collection of pus.

Chemotherapy, of course, for any infection on which it is satisfactorily active will in general take precedence over treatment by specific serum; it is also cheaper and more convenient.

In the nose and throat serotherapy is still of primary importance in the treatment of active diphtheria, and as an adjuvant to chemotherapy it may play a helpful role in acute pneumococcal, streptococcal and staphylococcal infections.

Diphtheria.—The diphtheria bacillus is not susceptible to chemotherapeutic agents, and in a case of diphtheria the administration of the antitoxin is still the first and most urgent requirement. The data regarding dosage are well known, but it may be stressed that the amount of toxicity exhibited by the patient is the important factor controlling dosage; also, that if the disease is over forty-eight hours, when first seen, the rather arbitrary figures of antitoxin usually indicated according to the type of lesion must be increased.

Pneumococcal infections.—The pneumococcus is a frequent pathogen in infective lesions of the nose, ear and throat. In localized acute infections, excluding involvement of bone, chemotherapy with sulphapyridine is now such an efficacious, cheap

and convenient remedy that the question of serum treatment does not arise. Complications give scope for the latter, but it must be emphasized that these are rare when chemotherapy is begun early and is sufficiently intensive. The complications in which specific antipneumococcic serum may be a useful adjuvant to chemotherapy in the field under discussion are bronchopneumonia (whether due to aspiration of infected material, or embolization of the pulmonary capillaries by infected thrombi), invasion of the blood-stream-septicæmia, and extension of the infection to the meninges. The commercial antipneumococcic sera available are mainly antibacterial in action; they have, as shown by Dick (1938), little antitoxic value. The production of antipneumococcic serum from rabbits represents a therapeutic advance compared with that produced by the immunization of horses (Horsfall and others, 1936, 1937). Rabbit's serum is cheaper and quicker to prepare, and can be made more concentrated, and the smaller size of its antibodies probably renders it more easily diffusible than specific horse serum. Commercial type-specific antipneumococcic sera prepared from rabbits can now be obtained for Types 1, 2 and 3 pneumococci and—more important, for the vast majority of the distinct 29 serological types—the so-called "higher types"—previously classified as the heterogenous Group 4. Specific antipneumococcic sera from the horse has not been practically available for these higher types, nor a clinically effective preparation for Type 3. In surgical procedures on the nose and throat, the aspiration of infected material from the pharynx is a risk liable to result in post-operative bronchopneumonia, and in the latter one of the higher type pneumococci is frequently the infecting organism (Whipple, 1918). There is great variation in the type of pneumococcus responsible for primary acute lesions in the ear, nose and throat but on the whole the lower types and especially Type 3 are common. Treatment with serum necessitates accurate preliminary typing of the infecting pneumococcus and the use of its homologous serum. It is to be regarded as an adjuvant to appropriate chemotherapy, especially in severely ill and elderly patients for whom there is no doubt that a combination of these two forms of treatment in bronchopneumonia and in septicæmia makes for more rapid clinical improvement and a reduction in mortality rate. With Type 1 infections, serum may be more efficacious than sulphapyridine; the latter is preferable for Type 3. Serum should be given to all cases when there is no definite improvement after twenty-four to thirty-six hours of sulphapyridine therapy, or when the latter is badly tolerated.

In bronchopneumonia, 60,000 units (10 - 25 c.c., according to type) intravenously is to be regarded as a minimal initial dose for the higher type infections. With lower type infections, especially Type 3, it is advisable to give more. The dose should also be high when there has been invasion of the blood-stream from the local lesion and a positive blood culture is present. Subsequent dosage depends on clinical progress and evidence of blood infection. The value of antipneumococcic serum as an accessory to chemotherapy in pneumococcal meningitis is doubtful (Coleman, 1940), but with a mortality of 35% with sulphapyridine treatment, cases should at least be given the chance of any benefit from specific serum. It is possible that future results with the more diffusible rabbit's serum given both intravenously and intrathecally in combination with adequate sulphapyridine dosage may improve this somewhat dismal outlook.

Acute streptococcal infections.—Streptococcal antitoxin is available for use in infections with the hæmolytic (β-hæmolysis) streptococcus; the latter bears a heavy responsibility for acute lesions in the ear and throat. The scarlet fever syndrome is dependent on the action in a susceptible individual of the erythrogenic factor of hæmolytic streptococci usually located in the pharynx; they can be assigned by agglutination reactions to the various types defined by Griffith and there is no serological distinction between scarlatinal strains and hæmolytic streptococci isolated from other sources in man.

In mild cases of β-hæmolytic streptococcal infections adequate dosage with sulphanilamide or allied drug is on the whole very successful, and serum therapy is not required. For the early or primary toxæmia of scarlet fever the results of antitoxin alone are striking and preferable to chemotherapy; combined with the latter, complications are much less frequent. When toxæmia is a feature in other forms of acute hæmolytic streptococcal infections (particularly at the onset), the antitoxin is a useful adjuvant to chemotherapy as the latter is bacteriostatic in action and has no direct effect in reduc-

ing an existing toxic state. Serum may also be a valuable accessory to sulphanilamide if septicæmia threatens, or is present, and also when extension of the primary localized infection has occurred—streptococcal bronchopneumonia, meningitis, cellulitis. There is no convincing proof that the various other commercial types of streptococcal antitoxin are more efficacious than the scarlet fever antitoxin used generally for any infection caused by hæmolytic streptococci. Accurate standardization of streptococcal antitoxin is difficult. In moderate degrees of toxæmia, 10-20 c.c. (6,000-8,000 U.S.A. units) of the refined and concentrated product intramuscularly is a reasonable dose. A more concentrated commercial preparation which I personally have not yet used is now on the market. The amount is increased and a portion given intravenously in cases of marked toxicity, when septicæmia is present or there has been extension of the infection. Repeated injections may be required on subsequent days, controlled by the clinical condition and progress.

Acute staphylococcal infections.—The *Staphylococcus aureus* is a far less prevalent pathogen in acute lesions in the ear, nose and throat territory than the hæmolytic streptococcus or pneumococcus. The high mortality rate of staphylococcal septicæmia when it does occur, and the fact that as yet we have found no drug capable of affecting the organism as sulphanilamide affects the hæmolytic streptococcus, render any possible serotherapy of special importance. In severe acute infections the early use of staphylococcal antitoxin combined with chemotherapy does appear to be helpful by raising the patient's resistance (Valentine and Butler, 1939; Butler, 1940). Valentine has claimed that the leucocidin is the significant toxin, and also that most patients have a low antileucocidin content in their blood during the early days of a severe infection. The production of staphylococcal antitoxin with a high antileucocidin content is still in an experimental phase, but the commercial antitoxin contains variable amounts. 20,000 units of staphylococcal antitoxin (about 25 c.c.) intravenously, given as early as possible, is a wise adjunct to chemotherapy in a severe acute case liable to result in septicæmia; if the latter occurs, the dosage should be increased and repeated.

Attention must be drawn to a necessity common to all forms of specific serotherapy: A preliminary test for sensitivity to the foreign serum should be carried out on the patient before administration, and desensitization proceeded with forthwith if the result be positive. In using specific serum as an accessory treatment to chemotherapy when complications arise, care should be taken to confirm the bacteriology in the new lesion and to exclude the possibility of superinfection by a different species or strain of organism.

In hæmotherapy, the use of blood and blood derivatives constitutes a non-specific remedy, but seldom required in the field under discussion. In any surgical procedure in which blood loss is liable to be significant, pre-operative transfusion is indicated if the patient has a hæmoglobin percentage of 70 or under (Haldane); also, post-operative transfusion in a case exhibiting secondary anæmia from hæmorrhage will shorten the period of convalescence. 500 c.c. of fresh blood raises the hæmoglobin 10% in an average-sized adult and on this basis it is easy to calculate in a given case the amount of blood required to reach a satisfactory pre- or post-operative hæmoglobin level. Stored blood is now used in civilian practice. Up to fifteen days old its efficacy in raising hæmoglobin percentage and restoring oxygen-carrying capacity in cases of acute hæmorrhage (with or without shock) and in chronic secondary anæmia compares well with fresh blood. Over this period and up to twenty-five days these effects, whilst still present, diminish fairly rapidly with storage on account of the development of fragility in the conserved cells. The degree of fragility in carefully collected refrigerated blood to which glucose has been added does not assume serious proportions for at least three and a half weeks; after this time, hæmolysis quickly develops. The incidence of reactions with stored blood up to twenty-one days old shows no significant increase contrasted with the use of fresh blood. Jewesbury (1941) at the N.E. London Blood Supply Depot analysing the results of the administration of 700 bottles of stored blood (average age just under eleven days), used in 389 transfusions, found a reaction rate of 19·8% of which only 4·1% constituted a Grade 3 reaction—a definite rigor. In the London Blood Transfusion Service, pre-war, the total reaction rate with fresh blood was approximately 15%. Stored blood is of a rather larger volume than a corresponding amount of fresh citrated blood owing to the increased proportion of diluent necessary (120 c.c. to 420 c.c. of blood). In the technique of administering

blood in transfusion, present-day practice is to use a drip rate when the blood volume is static. Reactions due to speed are eliminated and the risk of overloading the circulation is minimized. In combating anæmia in patients with heart disease, it is advantageous to provide maximum oxygen-carrying power with minimal increase in the blood volume. This can be accomplished by the use of concentrated red cells (MacQuaide and Mollison, 1940)—prepared by mixing the red cells, after syphoning off the plasma, of blood, between four and seven days old, that has attained maximum sedimentation on standing in the refrigerator. Such concentrated suspensions of red cells have, volume for volume, double the hæmoglobin raising power of ordinary blood. A further indication for this preparation, applicable to the present discussion, is the treatment of anæmia resulting from chronic sepsis.

Small volume (250 - 300 c.c.) repeated transfusions with fresh blood are valuable as an accessory therapeutic measure in septicæmia, especially in hæmolytic streptococcal infections. These quantities help to control the associated anæmia, and increase the antibody content (e.g. complement) of the patient's blood without overloading the circulation. Blood which is stored for more than a few days rapidly deteriorates as regards functional leucocyte content, platelets and other clotting factors, and also immune bodies, specific or non-specific. Fresh blood is therefore indicated when it is desirable to help the patient with any of these, e.g. leucocytes in agranulocytosis (an occasional toxic effect of chemotherapy), platelets and other clotting factors in the thrombocytopenia, hæmophilia and other hæmorrhagic diatheses, and immune bodies in severe infections. An acute hæmolytic anæmia is rarely seen as a complication of sulphonamide therapy; for this, and for diseases of the hæmopoietic system generally, fresh blood is to be preferred.

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Mr. J. Angell James: Since the introduction of the sulphonamide group of drugs there have been by comparison relatively few advances in serotherapy and hæmotherapy. Previously chemotherapy was rarely used in laryngological and otological practice. Serotherapy provided the only specific treatment of proved efficiency, with hæmotherapy as an adjuvant method. Chemotherapy with the sulphonamide group has now almost supplanted the other two methods in the treatment of suitable infections.

I propose first to consider some of the more important principles to be observed in the use of these methods, and secondly to give the results of treatment of series of cases before and after the introduction of the new drugs.

(1) All the sulphonamide group produce serious toxic reactions and should not be used for trivial infections.

(2) General chemotherapy is much more successful in acute than in chronic infections, presumably because the organisms are more accessible from the blood-stream in the acute case, and because more prolonged action seems necessary in the chronic case, and suitable concentrations cannot be maintained for a sufficient length of time with safety.

(3) Local chemotherapy which was earlier considered to be of little or no value is now proving successful in chronic as well as in acute infections. Jensen, Johnsrud and Nelson (1939) first described successful experimental results in the treatment of infection by local implantation. There was a discussion on chemotherapy and wound infection at a meeting of the Section of Therapeutics and Pharmacology of the Royal Society of Medicine in February last, when several speakers described successful local

treatment of septic wounds with sulphonamides (*Proc. Roy. Soc. Med.*, **34**, 337, Sect. Therap., 11). Fleming's (1940) observations that the action of these drugs is inhibited by the presence of peptones and bacteria is important, but this effect may be overcome by overwhelming concentration of the drugs. This can only be obtained safely by local application where surgical drainage has been established. Accessible wounds, mastoid cavities at the time of operation and radical mastoid cavities that have failed to dry up, accessory nasal sinuses and the middle ear, after thorough irrigation and cleaning, offer suitable conditions for the local method of treatment.

With local treatment only, there is insufficient absorption into the blood-stream to cause any severe toxic reaction. Concentrations up to 1·5 mgm. per 100 c.c. have been reported, Hawking (1941*a*). The highest blood concentration from local application to the ear or sinuses in my cases has been 0·9 mgm. per 100 c.c., and I have had no case in which any toxic reaction has been noted, where only local application was used. Local application should therefore be preferred to general where suitable conditions occur.

In choosing a local application the following points have to be remembered. Success depends on maintaining a high concentration for three to seven days of the drug which is known to be active against the organism concerned. The drug must be in close contact with a surface sufficiently moist to dissolve it, and pus must not be allowed to interfere. Sulphanilamide is highly soluble, will produce a concentration of 1,500 mgm. per 100 c.c., but is only fully active against the hæmolytic streptococcus; it is absorbed in one to two days. Sulphapyridine is relatively insoluble (only 42 mgm. per 100 c.c. at 37° C.), Hawking (1941*b*), and in mastoid cavities I have found it still present after two weeks; it tends to inhibit the formation of granulation tissue. It is active against hæmolytic streptococcus, pneumococcus and staphylococcus. Sulphathiazole is soluble (104 mgm. per 100 c.c. at 37° C.), it has persisted for a week in mastoid wounds and appears to have no ill-effect on granulations. It is active against the same group of organisms as sulphapyridine, but is much more active against staphylococcus, *B. proteus* and Hoffmann's bacillus, while probably less active than the other two against hæmolytic streptococcus. I have had no opportunity of trying sulphadiazine, but it is said to be active also against *B. friedländer* (Feinstone, *et al.*, 1940).

A mixture of sulphanilamide and sulphathiazole appears to be the most suitable powder, unless repeated applications can be made. It combines the advantages of early high concentration with prolonged action against the largest number of organisms. This is important where it has not been possible to identify the infecting organism, for in my series pneumococci have been present in the middle ear in 8%, *Staphylococcus aureus* in 24% of cases of otitis media. Since filling mastoid cavities with this powder at the time of operation there has been no subsequent gross suppuration in the wounds, and cultures taken at intervals have remained sterile. The wounds were first carefully prepared by syringing with peroxide and then hot saline, and sucking dry, in order to render them as clean and dry as possible. The first case with a widely pneumatized mastoid and large subperiosteal abscess was soundly healed in twelve days from the operation. In every case the temperature has fallen to normal on the day following the operation, and in only one case did it rise again, and that was to a temperature of 100° at night for three days a week later. Previously I had tried the post-operative administration of sulphonamide drugs by mouth, without any conclusive results.

Encouraged by this apparent success I tried sulphathiazole powder in four cases of radical mastoid cavities which had failed to heal, in each case in spite of prolonged treatment. Their durations were five years, twenty-seven years, twelve years and eight years. The organisms present were *Staphylococcus aureus*, streptococci, *B. proteus* and diphtheroids. In each case the ear was dry and apparently healed in a week after commencing treatment. The series is much too small and too recent for any definite conclusions to be drawn. On the other hand Herrell and Brown (1940) report two cases of wound treatment with sulphathiazole following external spheno-ethmoidectomy with no benefit.

For local treatment in the nose, antiseptic snuffs containing sulphathiazole or penicillin have been suggested (Delafield, Straker and Topley, 1941), but if the important principle of prolonged action is to be observed frequent application will be necessary, because of the rapid removal of the preparation by ciliary action. Their results show

that the snuff may lessen the frequency of effective invasion of the nose or nasopharynx.

Carrying these principles to the treatment of sinusitis I have injected infected antra and ethmoids with a paste consisting of:

Sulphanilamide 2 / Sulphathiazole 1 } 2 grm.

Starch 0·25 grm. Water to 10 c.c.

prepared and sterilized by the pharmacists at the Bristol Royal Infirmary[1] (at first I used sulphapyridine in tragacanth). In one case of a child aged 9 years with the right antrum and ethmoid full of pus, the sinuses were clear and radiographically normal, and the child clinically cured three weeks after one lavage and application of the paste. This case had previously been washed out with proflavine without any improvement. The organism present was a pneumococcus. I have made this paste radio-opaque with barium, and have taken skiagrams at intervals after filling the antrum. It persists for one week in quantity sufficient to recognize in the skiagram. It is sufficiently fluid to be injected quite easily with a Watson-Williams syringe. So far only a few cases have been treated.

In order to compare results of treatment I have analysed a group of cases of acute suppurative otitis media and a group of acute sinusitis seen during three years before 1936, and during the years 1938-40 inclusive. The cases include those seen at the Bristol Children's Hospital and in my private practice.

Acute nasal accessory sinusitis.—A total of 210 cases was seen.

In the pre-sulphonamide group, 42% required a sinus puncture, 25% required an operation.

In the post-sulphonamide group, 14% required sinus puncture, 7% required an operation.

There was thus a reduction by 66% of sinus punctures, by 72% of sinus operations. The operations referred to were not performed in the acute stage except in one or two instances where the infection was spreading into surrounding tissues and serious complications had arisen.

Acute suppurative otitis media.—A total of 750 cases was seen.

In the pre-sulphonamide group 15% required a mastoid operation and of these 6% had either a gross superficial abscess or meningitis, or sinus thrombosis when first seen; leaving 9% of early cases.

In the post-sulphonamide group only 1·7% of those which came under treatment before a superficial abscess, meningitis or sinus thrombosis had occurred required an operation.

Bowers (1940) reports a reduction from 11% of operations for early untreated cases to 5·7% in treated cases. Horan and French (1940) report a reduction from 22·7% requiring operation in the untreated group to 3·4% in the treated group. It seems possible that the further reduction shown in my figures may be accounted for by the additional use of ultra-short-wave radiation.

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[1] The paste is prepared as follows: Mix the powders and make up to volume with water. Transfer to suitable vessels (30 c.c. beakers or the equivalent) with constant shaking, 10 c.c. in each vessel. Cap with cellophane and autoclave at 105° C. for one hour. When cool, cap with a dust cover, paper, or waterproof cellophane. Stir with a sterile rod immediately before use.

Mr. Norman Jory: In acute otitis media the infection is by *Streptococcus pyogenes* in about 60%, pneumococcus in about 17%, pneumococcus Type III in about 13%, and staphylococcus in about 6% of all cases. Rarely found are Friedländer's bacillus, *B. pyocyaneus* and *B. diphtheriæ*.

It was natural to use the appropriate antiserum in desperate cases, and with apparent good or even dramatic results. The difficulty was to provide a specific antiserum, bearing in mind the large number of groups and types of organism. Nor was the use without discomfort and risk to the patient. Certainly no good result was obtained in cases of meningitis; and in many others serum therapy served merely to occupy the attention of surgeon and patient while the latter's natural defences overcame or were overcome by the invading organism. Similar failure of serum therapy to cure puerperal sepsis has been recorded by workers in that field.

Ehrlich's salvarsan showed that the "sterilisatio magna" long sought by the research chemist might yet be a possibility. German chemists working on aniline dyes found their bactericidal power greater when a sulphonamide group was attached to the benzene ring. In 1934 prontosil was synthesized. In 1935 Domagk showed that this protected mice against a lethal dose of human streptococci. In 1936 Colebrook and Kenny confirmed that sulphonamide was the active element of prontosil.

The use of these drugs at Queen Charlotte's Hospital reduced the mortality rate in puerperal septicæmia from 22·6% to 5·5%. It was soon used in streptococcal otitic meningitis with dramatic results. The introduction of M & B 693 proved equally effective against pneumococci.

Whereas before prontosil the mortality in streptococcal meningitis was over 97% and in pneumococcal almost 100%, now it is almost nil. One case in which I recall failure was a patient already moribund on admission to hospital.

Thus indirectly the surgery of the "acute ear" has been revolutionized.

Not many years ago the tendency in this country was to operate early upon the mastoid, some even opening drum and mastoid at the same time, largely because they were unwilling to have meningitis or other uncontrollable complication develop while they, though not, be it emphasized, the patient's defence mechanism, remained inactive. Now the tendency is to operate later and later, and one is agreeably surprised at the number of cases which resolve eventually in spite of early alarming symptoms. This moral support by sulphonamides seems to me an unpublicized but very real benefit.

There is a growing tendency to begin treatment by sulphonamides earlier and earlier in the course of the infection.

I regret that, owing to war conditions, I have been unable to collect statistics from St. Bartholomew's Hospital. What is certain is that the number of operations for acute mastoiditis has been enormously reduced. Moreover it used to be taught that mastoid drainage was almost inevitable in acute otitis media following nasal operations, now it is hardly ever necessary.

Recently Jessiman has suggested that sulphonamides should replace orthodox treatment of acute otitis media, and of otitis externa hæmorrhagica. The criticism of such wholesale therapy by sulphonamides is that they are potentially dangerous drugs. Were they entirely innocuous it would be rational to give them early and continuously in acute infections of the upper respiratory tract, even before any spread to the middle ear. In the vast majority of patients no harm results; but in a small minority annoying or even dangerous complications arise. The commonest untoward reaction, fortunately trivial, is cyanosis, which in a recent case developed after 1 grm. only of sulphonamide.

At the other extreme is agranulocytosis, of which a small number of cases, mostly fatal, has been reported. It is advisable to examine the blood picture every three days after ten days' therapy. But considering the amount of sulphonamide prescribed—in St. Bartholomew's Hospital alone last year 15,000 ½-grm. tablets of sulphonamide, 10,000 ½-grm. tablets of sulphapyridine, 4 lb. of sulphonamide powder, as well as soluble compounds, were dispensed—the number of fatalities is infinitely small.

Drug fever is occasionally met with, while malaise, nausea, and vomiting are common, more especially with sulphapyridine. Other untoward reactions are headache, dizziness, lassitude, mental depression, breathlessness and skin rashes. Thus it will be seen that the drug may readily produce disturbing symptoms suggesting an intracranial complication.

Further, sulphapyridine and sulphathiazole are potentially toxic to the liver and kidneys, and should be used with caution in cases of pre-existing damage to those

organs. Doubtless newer less toxic compounds will be evolved. One such, sulphadiazine, is reported from the U.S.A. Until completely innocuous sulphonamides are available it is wrong to use them in every case.

We know that the vast majority of cases of acute otitis media, including those with symptoms and signs of mastoid involvement, resolve under the usual routine treatment. The risk of unpleasant sequelæ, though slight, is always present, and is greater if the therapy is unduly prolonged. There is no evidence that mastoid operation is more commonly required with selective than with wholesale administration of sulphonamides.

Exceptions to this rule are meningitis, in which sulphonamides should be pushed from the start, the mastoid process being drained only if it is the site of chronic infection or of undrained pus; labyrinthitis, in which there is now even less need for labyrinthotomy than hitherto; and so-called "mucosus" infections, which are so apt to produce unpleasant surprises. Why do some cases fail to respond? Success depends on the specificity of the drug for the infecting organism, an adequate concentration of the drug in the blood-stream, and free access of blood or other body fluid containing the drug to the site of infection.

Fleming has shown that sulphonamides do not act so well in the presence of very large numbers of bacteria, and their action is inhibited by the products of suppuration. So we cannot expect undrained collections of pus to resolve on sulphonamides alone. Drainage need not necessarily be as thorough as in the past.

Thus, a patient seen some time after a mastoid operation had signs and symptoms of petrositis. The administration of sulphonamides enabled the poorly draining petrous cells to resolve in a few days. This accords with the observation already made that most cases which would previously have required operation because of inadequate drainage through the meatus now resolve on chemotherapy alone. In some of the cases which have failed to resolve without mastoid drainage it has been noted at operation that large peripheral cells had been unable to drain freely because of some obstruction between them and the mastoid antrum.

Thrombosis of a large venous channel does not appear to respond to chemotherapy.

A soldier had been treated by the military authorities for acute otitis media, including the administration of sulphapyridine. He was sent home apparently better, but returned because of a large swelling behind the ear, and was sent to an E.M.S. Hospital. No details of his chemotherapy were available then or later. His general condition and mental state were very good. His lesion was a large subperiosteal abscess, containing about 3 oz. of streptococcal pus, arising from thrombosis of the mastoid emissary vein. The lateral sinus was laid open, and found to contain firm clot. Thinking further chemotherapy, plus drainage, might suffice I, mistakenly, did not remove all the clot. He appeared to make satisfactory progress after this operation, yet, suddenly, five days later, had a hæmoptysis and died.

Autopsy revealed a clot extending to the upper end of the internal jugular vein, and numerous abscesses in the lungs. This shows that, although thromboses in small veins will usually respond, those in large sinuses fail to do so; and this corresponds with the findings in puerperal septicæmia.

Mr. T. B. Layton said that inflammations of the middle-ear cleft must be studied bacteriologically. The term "acute and chronic" should be abandoned for "pharyngeal and cutaneous inflammations of the middle-ear cleft". The tube of broth into which a piece of infected material is dropped was therefore as essential a part of the mastoid operation as was the gouge with which it was removed.

Referring to Mr. Jory's case of the thrombosed sinus, it was with the thrombosed sinus that sulphonamide drugs were likely to cause difficulties in diagnosis by masking the symptoms without touching the disease. He did not believe that it was a question of a large or of a small vein, but a question of the presence or absence of an organism in the clot. If there was no organism in the clot, this was a physiological reaction and should be left alone. If there was an organism in the clot no symptoms would arise from it until the breaking down of the clot had extended to some point from which organisms get into the blood-stream, and give a sudden rise of temperature, or, according to the dosage, a rigor. If chemotherapeutic drugs were used in that type of case they would mask the only symptom which would help one in deciding an operation, and thus they might endanger the patient's life. He believed, therefore, that after acute mastoid operations chemotherapeutic drugs should not be given.

Mr. F. W. Watkyn-Thomas said that in assessing the results up to date of the sulphonamide treatment account must be taken of the point Mr. Jory had made; of the moral support that it gave by encouraging people to wait a little before plunging into the mastoid.

The second point was the question of intracranial complications. He was not convinced that these had diminished in frequency. That their mortality had diminished he admitted, and this to an extraordinary degree, but as to a diminution of frequency, Colonel Whitby had pointed out that the sulphonamides did not act very well in bone, and the extension of intracranial complications was through bone. Not only that but, as Mr. Layton had pointed out, there was undoubtedly a danger of masking the symptoms. This applied especially to cases of septic lateral sinus phlebitis. His own rule was that sulphonamides might be administered in the earliest stages of acute otitis media, but once it had become necessary to carry out a paracentesis the administration should stop, because if there was going to be any further spread it would be in the bone and in the very spot where the sulphonamides could not get at it.

The same thing applied even more strongly in any question of intracranial complication. After the mastoid operation had been done sulphonamide should not be administered until the surgeon was actually in a position to diagnose any complications; then, having dealt with the complication, either lateral sinus thrombosis or meningitis, to the extent of removing the focus, the drug should certainly be given.

There was one exception in the treatment of acute cases; namely, the fulminating cases occasionally encountered—fortunately not often—in which the attack started with sore throat, acute otitis media, tension and tenderness, and a swinging temperature all in the first few hours. Those cases nearly always came to a mastoid operation, and in the past the great difficulty for the surgeon had been to hold his hand and await a suitable moment. In such cases sulphonamides would enable them to tide over the first few days of the case and avoid the necessity of operating when infection was at its peak.

Finally, how were sulphonamides going to act in a severe influenzal epidemic of the kind which attacked the ear, as it did about every five or six years?

Mr. Terence Cawthorne said that it was in the treatment of meningitis that the most dramatic results of chemotherapy had been seen. Gray, in a survey of the world's literature between 1900 and 1934, discovered only 27 cases in which recovery from bacterial meningitis (other than meningococcal) had been recorded. Since the first reported recovery in which chemotherapy was employed in the summer of 1936 until the summer of 1939, he (Mr. Cawthorne) had noted 194 recoveries from bacterial meningitis (other than meningococcal). His own experience of bacterial otogenic meningitis had included two recoveries in the twelve years preceding the introduction of chemotherapy, both of which had been under the care of the late Mr. G. J. Jenkins, and since the introduction of chemotherapy he had had 9 recoveries out of 15 cases.

Another disease which could be mentioned in this connexion was osteomyelitis of the skull secondary to frontal sinus infection. Since the advent of chemotherapy he had had three such cases clear up without extensive operation. In each case simple drainage of a subcutaneous collection of pus had been sufficient, and in two of the cases some months later it had been necessary to remove some tiny flakes of dead bone. Before the moral support of chemotherapy was available it was difficult to avoid embarking upon extensive operations in such cases—the final result of which, to say the least of it, was uncertain.

Colonel Whitby had mentioned the draining of the primary focus and had said that this must be carried out in all cases of meningitis. He was not quite sure whether one could agree with that, because in cases of fulminating otogenic meningitis the infection seemed to rush through the preformed spaces of the midde-ear cleft to attack the meninges before there could be any question of bone disease. Any extensive bone surgery at this stage would be fatal. The great hope lay in early intensive chemotherapy, and at this stage the only local treatment that might be required would be paracentesis, and only that if there was evidence of fluid in the middle-ear cleft with an unruptured tympanic membrane.

One interesting aspect of the result of chemotherapy in meningitis was the possibility of a second attack of what was formerly a fatal disease. He had had under his care a

nurse who recovered from otogenic streptococcal meningitis under combined chemotherapy and surgery. Some eighteen months later she developed a second attack of meningitis following an infection in the operated ear, which this time proved to be pneumococcal. This cleared up with chemotherapy alone. He would like to ask Colonel Whitby if he thought that intensive chemotherapy over short periods was likely to be dangerous.

Mr. R. G. Macbeth asked Colonel Whitby whether the sulphonamides were of any use prophylactically before operating on a "cold" case. For various reasons one was sometimes asked to remove tonsils rather soon after an acute attack; and in such cases one had a fear of acute inflammation, or even septicæmia following too early intervention.

Col. L. E. H. Whitby (in reply to Mr. Macbeth), said that the value of these drugs in prophylaxis was always difficult to assess, but obstetricians considered that their prophylactic use was justifiable in any case which had been delivered under suspicious circumstances. The recommendation with regard to war wounds was that any case which was considered likely to develop a heavy infection, particularly gas gangrene, should receive a prophylactic course of sulphonamide by mouth. The case must be the same in otology and laryngology, and a reasonable prophylactic course occupying two to three days was justifiable. The risk was very small, and the course could always be expanded into a full treatment course if required. When septicæmia was likely these drugs should certainly be used prophylactically.

Mr. Cawthorne had asked about the dangers of prolonged courses of minimal doses. Certain people were sensitive to these drugs and it was these cases which gave rise to trouble. Some could not tolerate more than a gram or two of the drug without exhibiting skin rashes or perhaps granulocytopenia or even agranulocytosis. These people were outside the average. Ordinarily a course of seven to ten days on full doses was given, the total dose amounting to between 50 and 60 grm. as a maximum. If that had not achieved the desired result it was unwise to go further without an interval. It was not so much a question of amount as of time. People became sensitized when even minimal amounts were given over prolonged periods. With a course of 50 grm. occupying ten days there was less likely to be trouble than by giving the same total amount over a period of a month. The time factor just as much as the total amount was important.

The incidence of the complications sprang very much more to the mind on account of their emphasis in the medical press than on account of the actual number of cases which had exhibited such complications.

When advocating the surgical treatment of the primary focus in meningitis he was perhaps going a little outside his field. The cases which he had in mind were those of bulging ear drum in which paracentesis was necessary, but clinical judgment was necessary to decide whether the mastoid should also be cleared.

As to whether people treated with chemotherapeutic drugs had any antibodies: animals treated with sulphapyridine and thereby recovering from a pneumococcal infection were thereafter immune to a second inoculation with living bacteria. Thus a durable antibody resistance was formed, but this was not so in any marked degree in the case of the streptococcus. In other words, the durability of streptococcal resistance was extremely transient, that of pneumococcal resistance was more prolonged, but even so not over many months. There was thus something to be said for active immunization with vaccines, but such immunization against the streptococcus was very transient and the results often disappointing.

He had been much interested in the work of Mr. Angell James on local applications of these drugs in the sinuses and the mastoid cavity. The present view concerning the local application of the drugs to war wounds was that one must have a perfectly clean and even surface with no pockets and that no tags of necrotic tissue must be present. It was recommended that the drug should be applied at the time of débridement and the application should be in the form of a very fine powder kept moist with a saline dressing. The view was that if there were any pockets there was ample opportunity for the multiplication of organisms of the gas gangrene group, but those, of course, did not enter greatly into the field now under discussion. If, however, they

wanted good success in the region of the ear, nose and throat they should bear the principle in mind that the local application should be made to a cavity or wound to which complete access was possible in such a manner that the substance could be distributed evenly and properly and kept moist. This would ensure proper solution of the drug and sufficient local concentration. Local application to a wound heavily infected with the β-hæmolytic streptococcus did not ensure a blood concentration sufficient to prevent blood-stream invasion by the active organism. Experimental work which had been done on this subject had indicated that in order to prevent blood-stream invasion it was necessary to supplement the local application by oral therapy.

Sections of Laryngology and Otology

COMBINED ANNUAL MEETING

[*May* 2, 1941]

LARYNGOLOGICAL SESSION

Chairman—T. B. LAYTON, D.S.O., M.S

(President of the Section of Laryngology)

The Clinical Aspect of Lymphosarcoma of the Tonsil

By EDWARD D. D. DAVIS

SOME pathologists divide lymphosarcoma into two types: (*a*) The lymphocytic type in which the round cells predominate, and (*b*) the reticular-cell type in which the larger reticular cells are more in evidence and are of reticulo-endothelial origin.

From the practical point of view sections of the whole tonsil have to be carefully searched before lymphosarcoma can be excluded. The two characteristics which make identification possible are firstly, the round cells which appear to be larger and which have no definite arrangement as in the normal tonsil and secondly, the round cells which infiltrate the deeper layers of the surface epithelium and muscular tissue. The latter is said to be a distinguishing feature of lympho-epithelioma. However, from a clinical point of view, lympho-epithelioma and reticular-cell sarcoma behave in the same way as lymphosarcoma. The name lymphoma has been given to any growth of the lymphoid tissue and has been subdivided into malignant and benign lymphoma. The malignant lymphomas include lymphosarcoma, lymphadenoma, multiple myeloma and lymphatic leukæmia. Benign lymphomas are simple growths of the various collections of lymphoid tissue. I have seen only two such cases, one of the pharyngeal tonsil which disappeared with radium treatment and did not recur, the patient surviving many years without any secondary growths. The second patient had a mass of lymphoid tissue at the junction of the hard and soft palate, for which there was no cause. It disappeared spontaneously. A few years later a smooth rounded mass of lymphoid tissue appeared at the upper end of the trachea and subglottic region. A low tracheotomy was required. The growth was removed and the area treated with deep X-ray therapy. There has been no recurrence for three years and the tracheotomy tube was removed. Microscopically the tumour was difficult to distinguish from lymphosarcoma.

In my experience epitheliomas spread from neighbouring structures such as the pharynx, tongue or jaw and they are not included in this communication. Lymphosarcoma of the tonsil is rare, and I can find the notes of only fourteen cases occurring over a period of twenty-five years. Munro Black gave brief notes of seven cases in his Hunterian Lecture delivered before the Royal College of Surgeons of England on January 26, 1938 (*J. Laryng. & Otol.*, **53**, 225).

There are three clinical types of lymphosarcoma of the tonsil. The first and commonest type is a sudden and rapid enlargement of one tonsil with an equally rapid enlargement of the corresponding lymphatic glands of the neck in a patient about the age of 40, or in later life. The tonsil is soft, friable, bleeds freely, the capsule is almost absent and, for this reason, enucleation is difficult. A section of the tonsil is sometimes stated to be normal but within a few weeks the glands in the neck increase in size and nodules of

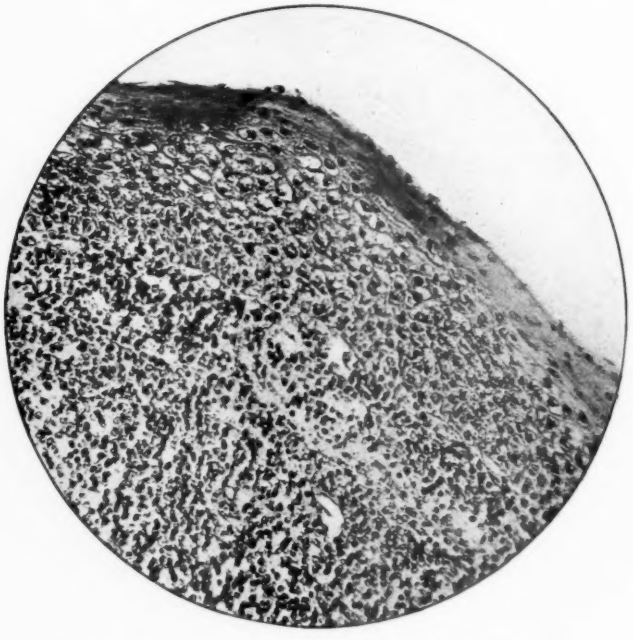

FIG. 1.—Lymphosarcoma of tonsil. Type I (× 200).

lymphoid tissue appear in the tonsil fossa, quickly forming a tumour. In these cases a further careful search of the section of the tonsil reveals evidence of lymphosarcoma. Examination of a section of the whole of the tonsil, and not a small piece of it, is essential. In my series there were eight cases of this type. In Munro Black's series six appear to be of this type.

The second type, of which there were four cases, closely resembled severe Vincent's angina when first seen. The ulceration, at first superficial and confined to the tonsil area, later became very deep and extended to the surrounding structures. The patients were about the age of 40 and gave a history of tonsillitis some weeks before the ulceration was seen. The diagnosis of tonsillitis had been made by their doctors. The enlargement of the lymphatic glands of the neck is only slight and is not a distinctive feature. The breath is foul. Wassermann reaction, bacteriological tests, and blood-counts are all

negative, but if a sufficiently large piece of the floor of the ulcer is removed and examined, the section reveals a reticular-cell lymphosarcoma. The diagnosis is in doubt for some time and all the usual treatment, including intravenous salvarsan, is ineffectual. Unless radium treatment is given the patient dies quickly, sometimes with severe hæmorrhage.

It is highly probable that the second type of case begins as the first type, but the growth ulcerates more quickly and before the tumour formation is apparent. In two of these cases the ulceration occurred on both tonsils. In addition, it has been suggested that the growth spreads deeply in the tissues and then ulcerates.

FIG. 2.—Reticular-cell sarcoma. Type II (× 240).

The third type, of which there were two cases, showed a mass of enlarged glands in the neck. It was difficult to find the primary growth, but this becomes evident at a later date. Lymphosarcoma of the nasopharynx may resemble lymphosarcoma of the tonsil but in the former case the lymphatic glands at the angle of the jaw on both sides are enlarged, although the primary growth is hidden for some little time. Lymphosarcoma of the tonsil may also resemble lymphadenoma, and it is only when secondary growths occur that the real diagnosis is obtained.

All the cases of lymphosarcoma I have seen have died within eighteen months from the time the first symptoms appeared. A few of these received radium treatment, the results of which seemed at first to be almost miraculous. The primary growth and glands rapidly disappeared, but within twelve months the patients died of secondary growths in the chest or abdomen. Lymphosarcoma is well known to be very radio-sensitive so that the earliest possible diagnosis and early radium treatment should be successful.

Discussion.—R. SCOTT STEVENSON said that he been fortunate in spending seven years in almost daily contact with Dr. Jobson Horne, who was accustomed to be very critical of the pathologist who gave the name of sarcoma to what might be chronic inflammation.

He himself had seen only five cases of lymphosarcoma of the tonsil. Two treated by dissection followed by X-rays were alive and well, one after eight years and one after five years, one treated by the same method had been lost sight of, and two treated at a later period by radium beam therapy were both dead. He had been influenced by the work of Berven in sending patients for radium beam therapy as opposed to his few cases treated by dissection and subsequent X-rays, for Berven had a long series of successful cases dating back to 1923. But he wondered sometimes whether it was not a good thing to dissect out the primary tumour in those cases, especially when they could be recognized early—his first case had a history dating back only a week or so, thanks to an observant family doctor.

G. E. ARCHER said that not long ago he had a case of interest. The patient, a bank manager, had a much enlarged right tonsil with some enlargement of the cervical glands. It looked like a malignant growth in the tonsil, but there was only slight superficial ulceration. It was decided to remove the tonsil for examination. It enucleated perfectly and cleanly and there was no evidence of infiltration around it. On cutting into the tonsil a solid piece of matter of about ¼ in. in diameter was struck. It felt like a piece of stone. The pathologist's report on the tonsil was "hyperplastic tonsillar tissue with no suggestion of neoplasm". The *stone* was submitted to a geologist who said that the structure was perfectly homogeneous and certainly non-calcareous and suggested it was possibly part of a tooth plate. After this the glands subsided for a little and those in charge of the case were perhaps rather complacent until the glands began to enlarge again some three months later. A general surgeon, Professor Morley, then saw the case and said that the diagnosis was that of lymphosarcoma. The glands were removed and the patient was treated by radiation, but he died some twelve months afterwards.

W. A. MILL said that he had at the moment several cases of sarcoma under his care at the Royal Cancer Hospital, some of which had been sent him by other members of the Section. One was a tumour of the tonsil which was removed at St. George's; it was a large tonsil in a young man—probably under 30—and was found to be sarcoma after removal. It was removed by diathermy. The case was quite clean when he saw it, and there were no glands, but in spite of that the gland areas were treated with deep X-ray therapy. He had had him under observation now for two years and there had been no recurrence. He saw him every few months. He had another patient—a woman of 28 or so—who had a tumour starting in the tonsil fossa on the left side of the throat, and spreading, one continuous tumour, down the left side of the pharynx and across the pyriform fossa on to the back of the larynx, and both sides of the arytenoid region were very much enlarged. She was treated with deep X-ray therapy eighteen months or two years ago, and so far there had been no recurrence.

He had never seen any flare-up from taking a section, although as a precautionary measure a short radiation was often given before the biopsy was made, especially if the growth was in an inaccessible place, but he was not frightened of taking a section without the preliminary radiation. There were also a few other cases attending out-patients. All these were cases of reticular-cell sarcoma. Some had been treated by deep X-ray therapy and one or two by the 5-grm. radium "bomb". As far as one could see, the reticular-cell sarcomas responded readily to radiation, and the prognosis did not seem to be bad; but it was useless to say anything definite until they had been under observation for five years or so. The lymphocytic-cell sarcomas also responded very readily, but he thought they almost always recurred.

At the Cancer Hospital, lympho-epithelioma was regarded as a very great rarity.

V. E. NEGUS said that he had seen five or six of these cases. He had treated them in different ways—by implantation of radon seeds, the use of radium needles, and diathermy. He would now refer such a case to some suitable centre for deep X-ray treatment or teleradium—it did not matter which, provided the treatment was given by the protracted fractional method. If the tumour was rapidly growing that would be sufficient evidence to justify referring it for treatment. If the radiotherapist preferred to take a section later for record purposes, well and good, but it was not a necessity in deciding on treatment. Radiotherapy from a distance seemed reasonable because it covered not only the primary tumour but the gland-bearing area. Treatment of the intervening lymphatics was very important. The treatment might not save the patient's life, but the primary tumour would disappear, and there would not be the same ulceration as if it had been left, and the patient's end would be less painful than if the condition had not been treated at all.

He had seen a soldier sent back from France, before the evacuation, as a case of lymphosarcoma, with a large mass in one tonsil, which one hospital reported to be

" rock hard ". It was an enormous tonsillolith about the size of the thumb and was expressed readily. It had caused inflammatory changes.

E. D. D. DAVIS (in reply) agreed that lymphosarcoma was very rare. He had collected his series of cases over at least twenty-five years. He felt certain that these cases, by whatever term described, were growths. The characteristic " miraculous " disappearance with radium treatment was entirely different from what occurred in an ordinary carcinoma. To take a section was only by way of confirmation of the diagnosis, which must be made on clinical grounds.

Direct Wound of Larynx.—F. C. W. CAPPS.

This man, aged 48, received a wound near the larynx on March 19, 1941, and the foreign body was removed on March 22. The voice was only a very poor whisper, he could cough, and the cords moved well. The voice has gradually improved, and the external swelling has diminished. The patient was examined by Mr. Watkyn-Thomas. He found a wound of entrance on the left side, with granulations above the cord, and a wound of exit on the right side through the centre of the right false cord. The cords moved well and the œdema was gradually subsiding. When seen by Mr. Capps on April 9, there was a very full false cord on the left side. The vocal cords moved normally, and the voice was surprisingly good.

Discussion.—V. E. NEGUS said that in the hospital where he worked they had received about 2,400 casualties, but there were only about two wounds of the larynx. No doubt among persons who were immediately killed, wounds of the larynx would be much more numerous, but these they did not see. In the case shown he thought the victim had been extremely lucky. The piece of incendiary bomb had gone right through but had left very few signs of damage. The only comparable case in his experience was a man whose larynx was hit with very little after-effect. Usually a hit on the larynx killed the patient by hitting other structures as well or by asphyxia. If the cartilages were wounded the chance of perichondritis was great. If the patient survived these various dangers he was liable to laryngeal stenosis. He had seen cases of self-inflicted wounds of the larynx and wounds sustained in motor accidents, and there might be and often was in such cases complete stenosis. The Semon Lecture was delivered on this subject some time ago by Professor Schmiegelow, whose method of holding a tube in place with silver wire was an excellent one, and to this the addition of a skin graft was of great importance. He thought that the interest to the laryngologist in these wounds was the liability to stenosis. Amongst the same 2,400 casualties there had been three cases of direct wounds of the trachea. Penetrating wounds of the trachea might do very little damage and cause practically no after-effects. The immediate danger was hæmorrhage and inspiration of blood, but the danger of perichondritis with stenosis was practically absent unless the wound was very extensive. He had seen several wounds of the neck in which the vagus or recurrent laryngeal nerve had been hit.

In reply to Mr. Capps, who asked whether it would be a good idea to use Professor Schmiegelow's technique to prevent stenosis, Mr. Negus said that one of the necessities was to wait until all perichondritis had subsided. If the patient had obstruction he would prefer a low tracheotomy and would wait two or three months before operating. The final result was very much better than if one were precipitate and operated at once.

R. SCOTT STEVENSON said that the French surgeon Despons, who had wide experience of laryngeal wounds, insisted that every case of injury to the larynx, even if comparatively slight, should have a tracheotomy done at once because such an injury might cause glottic œdema. In the last war the speaker saw a man whose larynx had been penetrated by a bullet, which had embedded itself in a vertebra; the surgeon left it where it was, and the larynx recovered without any stenosis.

NEVILLE YOUNG said that some months ago he saw an officer who had sustained multiple injuries, including a wound of the larynx, from a trench-mortar explosion. He had been in hospital for many weeks, and was complaining only of tiredness of the throat after speaking for long. Examination of the larynx showed it to be almost normal except for a small blue foreign body under the mucosa of the right cord, obviously metallic, about half the size of a gramophone needle. There was neither inflammation, nor fixity of the cord.

Carcinoma of the Œsophagus. Results of Deep X-Ray Treatment.—JOSEPHINE COLLIER.

Woman now aged 46 years and weighing 11 st. 10 lb. First seen May 1934. She had had six months' history of increasing difficulty in swallowing and loss of weight. On admission she was very emaciated, weighing 6 st. 8 lb., and swallowing only fluids. The X-ray

picture showed obstruction with filling defect beginning at the level of the 6th dorsal vertebra, and there was dilatation above the obstruction. Œsophagoscopy showed an ulcerated mass in the œsophagus, friable, and bleeding freely; the lumen was practically blocked. Biopsy revealed squamous-cell carcinoma. She had deep X-ray therapy at University College Hospital; 24 treatments from June 4 to July 5, 1934. There was gradual improvement in swallowing and steady increase in weight. A dry cough which came on four months after treatment has persisted with pain in the left side at times, especially during the winter.

Miss Collier showed X-ray photographs of the condition of obstruction when first seen and of the lungs as seen at present. The latter view showed fibrosis at the base of both lungs.

Section of Neurology

President—Geoffrey Jefferson, M.S.

[*April* 17, 1941]

Loss of Consciousness in Different Types of Head Injury

By Kenneth Eden, M.S., and J. W. Aldren Turner,, M.R.C.P.

It is seldom that there is opportunity to study the effects on consciousness of penetrating wounds of the brain. During the last eighteen months of war we have, therefore, taken special note of the amnesia of 200 consecutive cases of head injury of any type, admitted to Haywards Heath Neurological Centre.

It is not generally recognized that there is a wide variation in the effect on consciousness of various types of head injury. For instance Munro (1938) has recently stated: "Any significant cerebral injury in the sense that it is confined to the brain, in contradistinction to the skull and meninges, is always initiated by some degree of unconsciousness." In our view such a generalization as this is not strictly true of closed cerebral injury, and is certainly misleading when applied to open penetrating injuries of the brain.

The amnesia of cerebral injury.—In determining the duration of amnesia we have used the criteria of Russell (1932). By "retrograde amnesia" we, therefore, mean the interval between the last clearly remembered incident and the time of the accident. If the patient is questioned during the early stages of recovery, this period may amount to several hours or even days, but it usually shortens rapidly to a brief but permanent interval of a few seconds or minutes. There are a number of cases of closed cerebral injury in our series in which the retrograde amnesia some months after the accident still remains an hour or more in duration. At the moment it is uncertain whether this prolonged period of amnesia will persist, or whether it will eventually contract further.

We apply the term "post-traumatic amnesia" to the period of unconsciousness which follows the accident and is estimated by the interval between the moment of injury and the first return of consecutive consciousness. It is rarely so absolute as the retrograde amnesia, and may be punctuated by fragmentary memories of incidents—the so-called "high lights". For instance, the patient may remember the application of a dressing, but have no further memory until waking in hospital some days later. This post-traumatic amnesia corresponds not only to the period of coma or stupor, but also to that of the restless automatism which so frequently follows a severe head injury.

TABLE I.—TOTAL CASES OF HEAD INJURY.

(1)	Closed cerebral injury with or without fracture (due to road accidents, heavy falls and blows)	98
(2)	Scalp wounds without fracture.. (due to blows or projectiles)	12
(3)	Open cerebral injury— (due to penetrating metal splinters, i.e. fragments of bomb and shell casing and bullets, &c.) :	
	(*a*) Superficial—cortical and subcortical	27
	(*b*) Deep—base of brain..	14
(4)	Compound fractures—due to	
	(*a*) Massive violence—road accidents, falls and heavy blows	15
	(*b*) Projectiles—fragments of bomb and shell casing, glass and missiles, bullets, &c., without penetration of brain	34
		200

Closed cerebral injury.—The brief period of unconsciousness which usually results from a massive blow to the head, such as a falling beam or the impact of the head on the ground, is termed "concussion". Trotter defined concussion as "An instantaneous loss of consciousness, which is recoverable, and is not caused by any constant gross pathological changes". He stressed the fact that it is essentially a transient state, lasting a few seconds or minutes, and is followed by rapid return of full consciousness without clinical signs of focal damage to the brain. However one may interpret the pathological significance of concussion, in our view it is an accurate description of a clinical state, and we therefore propose to retain the term.

TABLE II.—TOTAL CASES OF CLOSED CEREBRAL INJURY.

		O	Secs.	Mins.	Hours	Days	Weeks
Number of cases, 98	Retrograde amnesia ..	5	45	35	8	0	0
	Post-traumatic amnesia	*1	3	25	42	19	8

5 cases were sleeping when injured and have no R.A.

**See* Case I.

It is evident from an inspection of Table II that a considerable proportion of the cases of closed cerebral injury in this series had a post-traumatic amnesia lasting more than a few minutes; in some it was prolonged for several hours, days or weeks. In many of these cases there were signs of focal damage to the brain, such as hemiparesis, hemianopia, or aphasia, with blood-staining of the cerebrospinal fluid. For these cases of prolonged post-traumatic amnesia, and those with signs of focal damage to the brain, we employ the term "cerebral contusion". We visualize this condition as a bruising of the brain, occurring principally near the area of skull struck, or by *contre-coup* violence, at the opposite pole.

In general, the amnesia of cerebral concussion and contusion in closed injuries of the brain is inseparable. It is only rarely in this type of injury that concussion is absent, and the effects of contusion can be observed as an isolated phenomenon, such as in the following case:

Case I.—A retired major, aged 61, was knocked down by a bicycle. He remembered striking his head, and subsequently getting up and walking home. Next morning, he was admitted to hospital, and was found to be confused and disorientated, with a left hemiparesis. The C.S.F. was blood-stained at a pressure of 140 mm. of water. He remained in this state for forty-eight hours, and because of the possibility of an intracranial hæmatoma, bilateral trephine holes were cut and the surface of the brain was explored. As no blood-clot was found, the brain was needled, and air was introduced into the ventricles, showing a normal ventricular system. Recovery was slow, but in about six weeks he returned to a normal mental state. During the period of recovery he was found to have a left homonymous hemianopia, which, however, cleared up together with the hemiparesis. At the time of discharge he was able to give a full and

coherent account of the accident, but had no memory of incidents for a week after going to bed on the night of the accident.

There was clear evidence in this case of localized damage to the brain, although there was no fracture and no concussion. The possibility of an intracranial hæmatoma, which had been suggested by the delayed onset of focal signs of cerebral damage, was excluded by exploration and ventriculography. In view of the absence of an intracranial hæmatoma and the eventual complete recovery without residual signs, we regard this case as an example of focal contusion without concussion.

Scalp wounds with cerebral injury.—This syndrome of "focal contusion without concussion" though rare in the massive closed injuries to the brain, is not uncommon in association with minor scalp wounds due to projectiles. The frequency with which signs of cerebral damage are found as a result of apparently trivial scalp wounds, has been emphasized by Jefferson (1919). Too frequently, concussion is regarded as the principal evidence of cerebral damage in such cases, and the complication of focal contusion is overlooked. There were only twelve cases of simple scalp wound in this series, but in three of them there was evidence of cerebral contusion, the wound in each case being due to a projectile. The following case is the most striking example:

Case II.—A boy of 13 was struck on the left side of the head by a bomb fragment. He remembered the blow and the blood flowing from a small scalp wound, but a few minutes later he lost consciousness for several hours. On admission to hospital three days later, there was a small left temporo-parietal scalp wound without X-ray evidence of a fracture of the skull, early papillœdema, some receptive aphasia, and a right extensor plantar response. During the next twenty-four hours he became more drowsy, with a falling pulse, and a C.S.F. pressure of 300 mm. of water. The C.S.F. was yellow in colour. In view of the possibility of an intracranial hæmatoma, bilateral trephine holes were cut and the surface of the brain was explored, but with negative findings. For a further four days the drowsiness increased and he developed jargon aphasia, a hemiparesis, and a right lower quadrantic hemianopia. His condition then took a turn for the better, and on dehydration therapy alone he made a slow but complete recovery without residual signs.

Unfortunately in this case, the brain was not needled and no ventriculogram was performed, so that it is impossible to exclude the existence of an intracranial hæmatoma. In view, however, of the rapid and complete spontaneous recovery, we feel it is probable that this was, like the preceding case, an example of focal contusion without concussion.

Both these cases show clearly that local damage to the brain may occur in the absence of concussion, a state of affairs even more clearly illustrated by cases of open cerebral injury.

Open cerebral injury.—In considering the effect on consciousness of open injury to the brain, we have divided the cases into two main groups, those due to the penetration of foreign bodies such as fragments of bomb or shell casing and bullets, and those due to compound fracture of the skull without penetration of the brain by metallic fragments.

Wounds of the brain with penetration by metal splinters.—In about two-thirds of the cases of penetrating injury of the brain, the foreign body was lodged superficially in the cerebral hemispheres; in the others it had penetrated deeply into the region of the basal ganglia or across to the opposite hemisphere. These deep injuries we have separated as a special group.

TABLE III.—TOTAL CASES OF OPEN CEREBRAL INJURY DUE TO SUPERFICIAL PENETRATING METAL SPLINTERS.

		0	Secs.	Mins.	Hours	Days	Weeks
Number of cases, 27	Retrograde amnesia ..	14	9	3	0	0	0
	Post-traumatic amnesia	10	4	2	6	4	1
	1 case was sleeping when injured and had no R.A.						
	In 10 cases there was no R.A. and no P.T.A.						

TOTAL CASES OF OPEN CEREBRAL INJURY DUE TO DEEPLY PENETRATING METAL SPLINTERS.

		0	Secs.	Mins.	Hours	Days	Weeks
Number of cases, 14	Retrograde amnesia ..	0	4	0	0	1	0
	Post-traumatic amnesia	0	0	0	1	3	1
	9 cases in coma terminating in death (no R.A. or P.T.A.).						

It may be seen from Table III that a third of the cases of superficial penetrating injury of the brain had no loss of consciousness, and that many others had only a brief retrograde amnesia or none at all, with a momentary post-traumatic amnesia. The following are typical examples of penetrating injury to the brain without loss of consciousness:

Case III.—A Polish pilot aged 25, flying a fighter plane at 20,000 ft. was hit in the head by a fragment of cannon shell from an enemy plane. He remembered the blow, but brought his plane down successfully. There was a wound of the left parietal region with scattered fragments of metal lying superficially in the left cerebral hemisphere. He had a severe right hemiparesis with cortical sensory defect, which cleared up slowly following débridement of the wound.

Case IV.—A factory worker, aged 18, sustained a small right parietal wound during an air raid. He remembered all the details of the blow, but took little notice of it and continued to work. Five days later he developed Jacksonian epileptic attacks starting in the left hand, and was then admitted to hospital. There was a fragment of metal 2 cm. across, lying in the cortex under the wound. This was removed; the wound rapidly healed, and a slight sensory defect in the left hand cleared up.

In contrast to cases such as these, there are other cases of superficial penetrating wound of the brain with definite amnesia, such as the following:

Case V.—A naval officer, aged 34, was injured when a bomb exploded on his ship. He remembered hearing the bomb falling, but not the explosion, and no more till he awoke in hospital three days later. He had a penetrating injury of the left temporal region with a fragment of metal lodged in the cortex, severe mixed aphasia and hemiparesis. The foreign body was removed and the wound healed slowly with gradual disappearance of the neurological signs.

Analysis of the cases of penetrating wound of the brain to show whether the size of the fragment, or the place where it pierced the cortex, is the factor which determined unconsciousness, has given negative results. It seems probable, however, that when there is immediate unconsciousness, it is caused, not by the penetration of the missile, but by the superadded effect of a massive blow to the skull. This might be caused by exposure to flying debris when a bomb explodes nearby, or as a result of a heavy fall to the ground. The effects on unconsciousness of two such injuries are occasionally separated by a distinct interval as in the following case. This, however, is the exception rather than the rule.

Case VI.—A sergeant rear-gunner, aged 26, was hit in the right frontal region by a machine-gun bullet, in aerial combat. He remembered this blow, but a few minutes later the aeroplane crashed, and he had no further memory till waking on the boat to England ten days afterwards.

Evidently this patient was not rendered unconscious by the penetrating injury to the brain, but some few minutes later received a superadded massive injury, when the aeroplane crashed, which resulted in prolonged unconsciousness. We have purposely avoided the suggestion that "blast" may be responsible for causing concussion in penetrating wounds for it is impossible when taking a history at a base hospital to ascertain the exact relationship of the patient to the explosion.

The delayed onset of unconsciousness cannot always, however, be explained on the basis of a second injury, though it may be attributable to the effects of a complication such as hæmorrhage.

Case VII.—An A.A. gunner, aged 22, was admitted to hospital twenty-four hours after sustaining a punctured wound of the left parietal region, during an air raid. On admission, he was in deep coma, and remained so for many days. There was a right hemiparesis and the C.S.F. was blood-stained at a pressure of 310 mm. of water. A metal fragment was lodged 2-3 in. in the cerebral hemisphere, and the wound which had been excised, was healing. The patient was left untouched for fourteen days, during which time the coma persisted; the wound, which was healed, was then re-explored. At operation a large hæmatoma was found in the wound track and was evacuated. He subsequently regained consciousness. In time the paralysis cleared up, a homonymous hemianopia rapidly disappeared, and before discharge he was able to give a clear account of the accident. He remembered the explosion, the blow to the head and subsequently running to the first-aid post for treatment. Following this he had no memory until waking in hospital a fortnight later.

In contrast to the superficial penetrating injuries, prolonged unconsciousness is the rule in the deeper wounds of the base of the brain. Nine out of fourteen of these cases died in coma, while there was only one case with a post-traumatic amnesia as short as a few hours. To what extent such factors as hæmorrhage into the ventricles or the depths of the brain, and infection, determine these findings, is uncertain, but it seems probable that the distribution of the swelling in the basal part of the brain is significant. Without further information on these points it is impossible to speculate on the factors determining unconsciousness in these cases.

Compound fractures of the skull.—A considerable proportion of open injuries to the skull are depressed fractures without penetration of the brain by metal splinters, although fragments of bone may have been driven a variable depth inwards. We have placed these cases in a separate group because the mechanism of injury is often different from that in the last group. It is, in fact, difficult in some cases to determine the nature of the missile.

TABLE IV.—COMPOUND FRACTURES OF THE SKULL.

(Without Penetration of the Brain by Foreign Bodies.)

(1) *Massive violence (road accidents, heavy blows and falls).*

		0	Secs.	Mins.	Hours	Days	Weeks
Number of cases, 15	Retrograde amnesia ..	0	3	8	1	0	0
	Post-traumatic amnesia	0	0	3	1	6	3
	1 case was sleeping when injured and had no R.A.						
	2 cases in coma terminating in death (no R.A. or P.T.A.).						

(2) *Low velocity projectiles (small fragments of metal lodging in bone, flying pebbles, &c.).*

Number of cases 11, of which 10 had no R.A. or P.T.A.
1 case had 5 mins. of P.T.A. without R.A.

(3) *Unknown missiles (? flying masonry, &c.).*

		0	Secs.	Mins.	Hours	Days	Weeks
Number of cases, 20	Retrograde amnesia ..	6	8	4	0	0	0
	Post-traumatic amnesia	4	1	4	7	3	0
	1 case in coma terminating in death (no R.A. or P.T.A.).						
	In 4 cases there was no R.A. or P.T.A.						
	1 case was sleeping when injured and had no R.A.						

(4) *Flying glass fragments with explosion*—3 cases.
2 cases had secs. of R.A. and mins. of P.T.A.
1 case had mins. of R.A. and hours of P.T.A.

In Table IV cases of compound fracture of the skull are divided into four groups: those known to be caused by massive violence such as road accidents and heavy falls, those due to small low velocity projectiles such as fragments of metal, pebbles, &c., which have lodged in the skull, those in which it is impossible to be sure of the nature of the missile, and lastly a small group of cases injured by showering of glass from an explosion.

With regard to the first group of these cases, little comment is necessary; they are similar in nature to the closed cerebral injuries from massive violence, and the effect on consciousness is correspondingly the same. Of the compound fractures caused by low velocity projectiles, the majority were small depressed fractures, in some cases with metal fragments lodged in the bone. Ten out of eleven cases had no amnesia, a finding comparable with that in the uncomplicated superficial penetrating injuries of the brain.

Case VIII.—A man of 34, while walking in the street heard a bomb explode and threw himself to the ground. He felt a blow to the head, got up and walked to a first-aid station. A metal splinter 1½ in. across, part of the casing of an oil bomb, was lodged in a small depressed fracture of the right parietal region. It was removed, and the patient made a good recovery.

Little can be said about the third group of compound fractures, for the nature of the missiles is uncertain. It seems probable, however, that these patients were mostly injured

by flying masonry or heavy fragments of metal, at low velocity. It is therefore not surprising that the majority had concussion. On the whole the wounds were extensive, with splintering of the bone in some cases, and showering of splinters into the brain.

The three cases of compound fracture of the skull caused by splinters of glass from an explosion have been placed in a separate group because of the distinctive nature of this injury. The following case will serve to describe it:

Case IX.—A girl of 23 was sitting in her bedroom during an air raid, when a land-mine exploded nearby. She did not remember hearing the explosion, but awoke to find herself still sitting in the chair, covered in blood. Her face and neck were riddled with fragments of glass which had cut the left jugular vein and the vagus nerve. There was a compound fracture of the left parietal region. She was confused and disorientated and the cerebrospinal fluid was blood-stained at a pressure of 150 mm. of water. When the fracture was explored at operation, the bone was found to be penetrated by multiple tiny fragments of glass which had not opened the dura. All the glass was removed and after débridement the wound was closed. The patient made an uneventful recovery.

In this type of case there is a severe blow to the head from numerous fragments of flying glass, some of which pierce the skull and lodge in the bone. The effect on consciousness is comparable to that of a massive blow from a heavy object, with resulting concussion and contusion.

Discussion.—In this study we have shown that there are two possible effects on the brain of a blow to the head. The first—concussion—is an instantaneous but transient period of unconsciousness, usually with retrograde amnesia, and unassociated with other signs of damage to the brain. The second—contusion—is characterized by localized signs of brain injury, blood-staining of the cerebrospinal fluid, and in some cases only, unconsciousness, which may be delayed in onset for several minutes or hours.

Concussion occurs nearly always as a result of massive violence to the head. This may take the form of a heavy fall in which the head strikes a hard flat surface such as the ground, or a blow to the head from a large missile at a relatively low velocity, such as a flying brick or falling beam. If the violence is sufficient to overcome the normal elasticity of the skull, either a simple fracture or a compound splintered fracture results, but this does not affect the concussion. Small objects—such as fragments of bomb casing—even though they strike the skull at a velocity sufficient to cause penetration, frequently do not result in concussion.

Whether concussion be visualized as a " temporary deformation of the skull ", as Trotter described it, or as a " jarring effect ", in the words of Russell, it is clear that the force is transmitted through a large part of the skull, and makes itself felt on the brain as a whole. The factor which most determines the presence of this generalized shaking-up effect on the brain is the size of the object striking the skull, or conversely the surface area involved in the injury. Providing that there is adequate momentum, a blow involving a large part of the skull causes concussion, whereas a small localized impact does not.

Contusion, on the other hand, which we regard as bruising of the brain, occurs in all types of head injury. Massive violence to a large area of the skull may cause widespread contusion of the brain, with resulting unconsciousness, but since concussion is also present in these cases, it is difficult to separate the amnesia in the two conditions. Unlike concussion, however, contusion is also produced by localized injury to the head, and in such cases it is possible to observe its effects, uncomplicated by concussion.

A small fragment of bomb casing striking the skull at high velocity will perforate it and penetrate the brain; at a lower velocity it will cause only a small depressed fracture and either lodge in the bone or drop off the skull; while if the velocity is very low it will cause only a superficial scalp wound without a fracture. Contusion may occur as a result of any of these injuries. The only one, however, which constantly produces unconsciousness is a wound penetrating the basal parts of the brain; in the remaining types there is frequently no loss of consciousness. This evidence, imperfect as it is, suggests that the basal parts of the brain are more concerned with consciousness than any one part of the cortex.

In severe cases of cerebral contusion there may be a slow delayed onset of unconsciousness. Such delayed unconsciousness naturally gives rise to the suspicion of intracranial

bleeding, particularly when there is evidence of focal damage to the brain. In such cases it is seldom possible to be sure of the diagnosis until the possibility of an intracranial hæmatoma has been excluded by exploration and needling of the brain.

Sometimes a massive blow to the head is superimposed on a penetrating injury. This may occur when there is a heavy fall to the ground at the time of the accident, or the head is struck by flying debris in addition to bomb splinters. In such cases concussion is present in addition to the usual evidence of a penetrating injury.

SUMMARY

(1) A series of 200 cases of different types of head injury, both closed and open, have been examined with reference to the loss of consciousness sustained.

(2) There are two different ways in which the brain may be injured by a blow to the head: there is a generalized effect in which the force is transmitted throughout the skull to the brain as a whole, which results in immediate unconsciousness—concussion; and a localized bruising effect, often with signs of focal damage to the brain—contusion. In the absence of concussion unconsciousness occurs only as a result of contusion of a severe degree, and may then be delayed in onset and prolonged in duration.

(3) Injuries due to massive violence, such as road accidents and heavy falls, commonly cause concussion, with or without contusion. In a large proportion of wounds due to projectiles and small missiles (including scalp wounds, depressed fractures and penetrating wounds of the brain), concussion is absent, even in the presence of contusion.

(4) Loss of consciousness following a penetrating wound of the brain may result from a superadded massive blow to the head, such as a fall to the ground, or a complication such as cerebral hæmorrhage; or it may indicate widespread contusion from a wound deep in the base of the brain.

(5) The important factor which determines the presence or absence of concussion in head injury is the area of skull struck, providing that there is adequate momentum.

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Experimental Concussion

By Major D. E. DENNY-BROWN and Major W. RITCHIE RUSSELL

ABSTRACT.—The various hypotheses of the mechanism of coma resulting from cerebral trauma are discussed. Experimental evidence shows that there are two kinds of transient abolition of cerebral function by trauma—acceleration concussion, and compression concussion. The former is a passing paralysis which occurs in all brain-stem mechanisms examined and is brought about at and beyond a threshold value of change in velocity. A lesser degree of change causes momentary depression of function, a greater degree prolongs the phase of paralysis before recovery occurs. Movement of the head is necessary for the usual kind of concussion to occur, as also for *contre-coup* injury. Compression concussion has much more selective incidence on the respiratory centre, and appears to require an extreme crushing injury or penetration of the skull by a relatively large object. Acceleration concussion is that accompanying closed head injury and is not accompanied by any significant change in C.S.F. pressure. The cerebral blood flow is very greatly increased in this variety owing to stimulation of the vagoglossopharyngeal nerves at the foramen magnum. With more severe blows subpial or intramedullary lesions may occur in this situation, indicating that distortion at the foramen magnum occurs. No evidence of vascular spasm or paralysis is found. An immediate brief rise of blood-pressure is due to stimulation of the vasomotor centre. Vagal effects may not appear until the traumatic paralysis of all centres begins to pass off. A delayed fall in blood-pressure lasting many minutes may follow severe vagal effects, and appears comparable to acute surgical shock as produced by intense stimulation of any other visceral nerve. Death

occurs from failure of blood-pressure, an intensification of shock with shallow respiration and intense constriction of viscera.

It is concluded that sudden failure of what has been called the veno-pressor system is important in death shortly following experimental concussion. No macroscopical lesions are found, and histological examination shows no change with ordinary tissue stains. The unconsciousness of coma is believed to be related to direct traumatic paralysis of the cortical neurones and if their sensitivity to physical violence is similar to that of anæsthetics, prolonged impairment of function from this cause alone is possible. Clinical observations were related in support of these conclusions.

(*Full text to be published in "Brain"*)

Section of Odontology

President—Evelyn Sprawson, M.C., D.Sc., L.R.C.P., M.R.C.S., L.D.S.

[*April* 28, 1941]

Experimental Investigation into the Early Effects of Various Filling Materials on the Human Pulp

By E. B. Manley, L.D.S.Manc.

This paper is not intended to represent a completed piece of research, but is a report on results so far obtained. Apart from difficulties brought about by present war conditions which have allowed only a certain stage in the investigations to be reached, the results of the experiments themselves have produced phenomena, the interpretation of which yet remains to be clearly established.

PURPOSE OF INVESTIGATION

The object of the investigation is to determine the nature and degree of reaction on the human pulp of various materials used in the filling of teeth. This work, together with the preliminary experimental work carried out on the teeth of dogs, is the logical outcome of the earlier work of Fish (1932), who established experimentally the fact that peripheral injury to the dentinal fibrils causes a reaction at their pulpal ends, the pulp tissue itself being affected to a degree corresponding to the severity of the injury. It was shown that this reaction is always strictly confined to the pulp surface of the injured tract of tubules. It never overlaps the uninjured tubules, and could, therefore, be regarded as a specific reaction to injury of the dentinal fibrils.

METHOD

Patients were selected from the Orthodontic Department in whom the extraction of the premolars was required. Sound teeth only were used, and cavities were prepared on the gingival third of the buccal surface. Prior to operation the teeth were isolated from mouth fluids. The same technique for cavity preparation was adopted as that used in the preliminary experiments on dogs, a "slow-motion" hand-piece with new burs being employed throughout. No anæsthetic was administered and careful note was made of any manifestation of undue sensitivity.

After the allotted period of time had elapsed the teeth were extracted under nitrous oxide. After extraction the apices of the roots were cut off to facilitate free access of reagents to the pulp. The teeth were then fixed, decalcified and embedded in paraffin. Serial sections were cut and stained with hæmatoxylin and eosin, Van Gieson, Mallory and Masson's stain.

Where possible one premolar tooth was used as control, but as any reaction is strictly confined to the pulpal end of the injured tubules, the cells above and below this area or on the opposite side of the pulp may themselves be considered as controls.

For purposes of comparison the same filling materials were used as in the experiments on dogs, viz. silver amalgam (6), silicate cements (5), zinc oxide and eugenol (6), and

copper oxyphosphate cement (3). The figures indicate the number of cavities filled with each material. The photomicrographs of the reaction are taken through the deepest part of the cavity.

DISCUSSION

In the preparation and filling of an experimental cavity both physical and chemical irritants can affect the tooth structure. The physical irritants produced are trauma and excessive heat which can be generated by a rapidly revolving bur. The chemical differences which exist between various filling materials introduce a factor of great clinical importance. Clinical evidence shows that silicate cements, for example, can cause death of the pulp, whereas zinc oxide and eugenol is successfully used as a sedative dressing. After the preparation of the cavity, filling materials in a plastic state come into contact with the cut ends of the dentinal fibrils, and it seems reasonable to suppose that these materials, chemically so dissimilar, would produce different effects on the pulp. In a preliminary investigation (Manley, 1936) where dogs were used as experimental animals, cavities in canine teeth were filled with zinc oxide and eugenol, silver amalgam, silicate cements and copper oxyphosphate cement. The results obtained showed that zinc oxide and eugenol caused no reaction and had no deleterious effect on the pulp. Silver amalgam, silicate cements and copper oxyphosphate cement gave marked reactions in the pulp, and their reactions had distinctive characteristics due to a difference in chemical composition. Cavities lined with zinc oxide and eugenol and filled with either amalgam or silicate cement produced no reaction. These results have since been substantially confirmed in America (Gurley and Van Huysen, 1937).

Experimental work on the human subject presents certain difficulties which do not arise in the case of dogs, where a general anæsthetic was used. A young patient will not tolerate too long a dental operation, however painless, and, accordingly, the temperament of the child influenced to some degree the size and depth of the cavity.

Other difficulties arose for which certain allowances should be made, and these call for some explanation. For example, most parents are quite willing for their children to have fillings inserted in teeth already doomed for extraction for orthodontic purposes, but the question of the length of time that must elapse between the time of filling and date of extraction presented unforeseen difficulties. The "stay of execution" (parents' conception) of fourteen days caused no difficulty, but for some reason or other suggested longer periods evoked mild opposition. However, by various means and through the loyal co-operation of our orthodontic surgeon, this difficulty was largely overcome, and periods varying between two and eight weeks were allowed to elapse before the teeth were extracted. This difficulty is in reality a distinct advantage. The variations in time between the insertion of the filling and the extraction of the teeth form interesting comparisons, and have allowed the early changes in the pulp to be observed.

Another, and more unfortunate, difficulty resulting from the present war conditions has been the loss of material through the evacuation of the patient during the waiting period, and also through actual air-raid casualties.

In order to determine the effect of any filling material by itself it is necessary to eliminate as far as possible two factors during cavity preparation—the traumatic effect of the drill, and bacterial infection through contamination with mouth fluids.

The effect on the pulp of traumatic stimuli produced by a rapidly revolving bur on the dentinal fibrils I consider to be most important. Let us assume that the pain caused by the drill during the cutting of a sensitive cavity has become intolerable to the patient. If, instead of resorting to the use of local anæsthesia, a slow-motion or reducing handpiece is substituted for the ordinary type, thus reducing the speed of the bur without detracting from the power of the engine, the cutting of the cavity can be resumed and completed in comparative comfort to the patient. This has been demonstrated repeatedly in the Conservation Department of the Birmingham Dental School. Pain caused by the drill is an indication of pulp irritation, and it may be assumed that the traumatic effect of the drill has been reduced to a minimum, if, without the use of anæsthesia, the cavity can be cut painlessly.

Bacterial infection through contamination with mouth fluids was eliminated by the use of rubber dam or other similar means.

The question of depth of cavity calls for some comment. Cavities of varying depths were prepared, although no scientific attempt was made to control this factor which must modify the degree of pulp reaction in so far as the distance of the site of injury

from the pulp varies. The structural relationship which exists between the dentine and pulp should, without recourse to animal experiments, justify the expectation that the nearer the pulp the stimulus is applied the greater will be the reaction.

In all the experiments about to be described cavities were cut in sound, healthy teeth. From a practical point of view, the criticism may be offered that in the ordinary way caries would be present, in consequence of which a reaction will have already occurred in the pulp as a result of bacterial infection. However, as has been pointed out previously, in the preparation of all carious cavities for filling, the cavity is extended well beyond the limits of the carious dentine, and new, healthy tubules are opened up. The filling material, therefore, would come into contact with the cut ends of healthy dentinal fibrils. This applies particularly to small cavities in the teeth of young people, the pulps of which will react most readily to injury, and it should be emphasized that it is to the teeth of young people that the practical side of this investigation should be more particularly directed.

DESCRIPTION OF EXPERIMENTS

I. *Silver amalgam.*—A definite type of reaction is seen to occur under cavities filled with silver amalgam.

Fig. 1 shows the reaction five weeks after filling. Calcification of the odontogenetic zone (O.Z.) has taken place; collagen fibres are being deposited with the commencement of secondary dentine (S.D.M.) formation. The odontoblasts (O.) are reduced in number and some show degenerative changes. Numerous capillaries have come into view.

Fig. 1*a* shows the normal odontogenetic zone and odontoblast layer below the cavity.

A sudden and more severe reaction under a larger and deeper cavity three weeks after filling is seen in fig. 2 and fig. 2*a*. Marked stimulation has ocurred causing hyperactivity of the cells. Calcific material (C.M.) has been deposited at the edge of the odontogenetic zone (O.Z.), which is still clearly visible, and has not become fully calcified. New matrix of secondary dentine (S.D.) is being laid down and numerous capillaries are present. The odontoblasts (O.) are greatly altered in appearance and at one point round-cell infiltration (R.C.) has occurred deeper in the pulp tissue. The normal odontogenetic zone (N.) and odontoblast layer is seen under the unaffected tubules away from the cavity.

Fig. 3, a high-power magnification of the reaction under another cavity three weeks after filling, illustrates the marked vascular changes that occur. Numerous capillaries (C.) have appeared in the odontoblast layer, the cells having become displaced. The odontogenetic zone has become completely calcified, but no secondary dentine has as yet formed.

II. *Silicate cements.*—A more serious type of reaction occurs under cavities filled with silicate cements, which are seen to produce a marked toxic effect on the pulp. In fig. 4 the white lines indicate the extent of the tract of tubules involved under a cavity six weeks after filling. At A, under the deepest part of the cavity, degeneration and destruction of the odontoblasts have taken place, many capillaries (C.) have invaded this area, and the pulp tissue underneath the damaged odontoblasts is invaded by round cells (R.C.). At B, under a less deep part of the cavity, secondary dentine (S.D.) has been laid down, and there is marked reduction in the number of odontoblasts. Normal odontoblasts (N.O.) are seen on the opposite side of the pulp. A higher magnification of A (fig. 4*a*) shows the destruction of the odontoblast layer, the presence of capillaries (C.) and the formation of an irregular deposit of new matrix (M.). The pulpal ends of the tubules of the primary dentine (P.D.) are calcified up. A higher magnification of B (fig. 4*b*) shows the secondary dentine laid down which contains few and irregularly formed tubules. The odontoblast layer is greatly reduced, the cells showing degenerative changes. A calcific barrier between the primary and secondary dentine is well defined.

Under a shallow cavity only two weeks after filling a marked reaction is seen to have taken place (fig. 5). Capillaries (C.) have come into view, and an area in the deeper part of the pulp is invaded by round cells (R.C.). Marked changes in the odontoblast layer have occurred. At one point (S.) spaces are seen due to the pushing apart of the odontoblasts by an intercellular accumulation of fluid. This is well illustrated in fig. 5*a*, a higher magnification of this area. Complete degeneration of the odontoblast cells is seen in the area D.O. Other cells are present, probably of an inflammatory nature. The appearance of these cells and the degenerated odontoblasts is well shown under high magnification (fig. 5*b*).

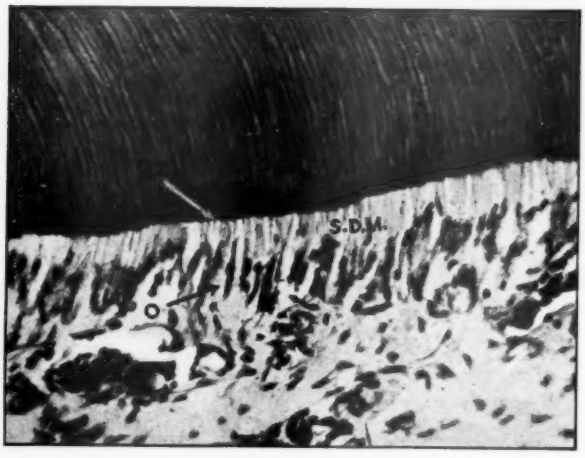

FIG. 1.—Photomicrograph × 300. Reaction under silver amalgam (5 weeks). Boy, aged 11. O.Z. = Odontogenetic zone. S.D.M. = Secondary dentine matrix. O. = Odontoblasts.

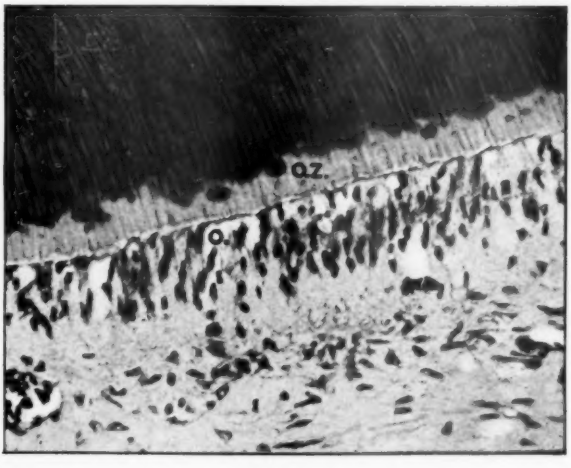

FIG. 1*a*.— × 300. Normal odontogenetic zone and odontoblast layer below reaction shown in fig. 1.

FIG. 2.—× 90. Reaction under silver amalgam (3 weeks). Boy, aged 12. C.M. = Calcific material. O.Z. = Odontogenetic zone. S.D. = Secondary dentine. O. = Odontoblasts. R.C. = Round cells. N. = Normal odontogenetic zone.

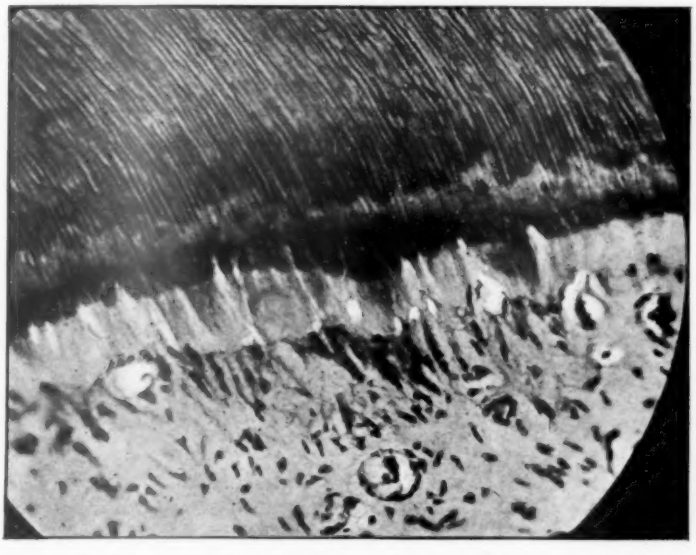

FIG. 2*a*.—× 250. Reaction under silver amalgam. Higher magnification of fig. 2, showing hurried deposition of calcific material. Outline of normal odontogenetic zone still visible.

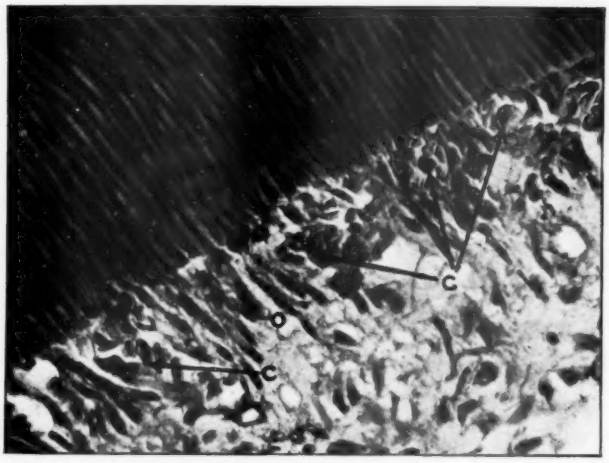

FIG. 3.—× 480. Reaction under silver amalgam (3 weeks). C. = Capillaries. O. = Odontoblasts.

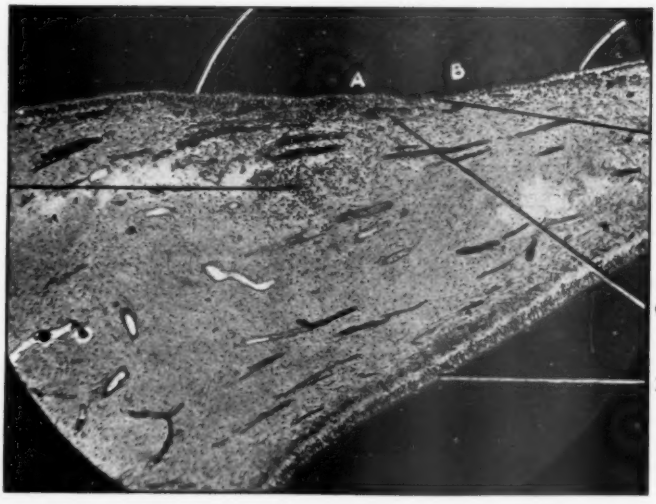

FIG. 4.—× 40. Reaction under silicate cement (6 weeks). Boy, aged 10. C. = Capillaries. R.C. = Round cells. S.D. = Secondary dentine. N.O. = Normal odontoblasts.

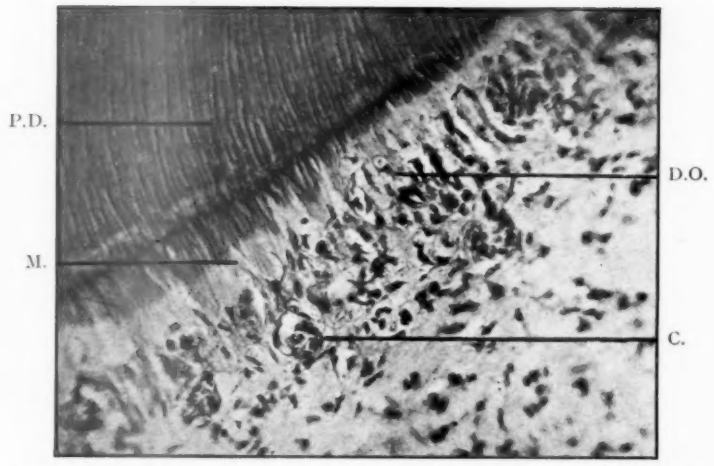

FIG. 4*a*.—× 300. Reaction under silicate cement. Higher magnification of area A, fig. 4. C. = Capillary. D.O. = Degenerated odontoblasts. M. = New matrix. P.D. = Primary dentine.

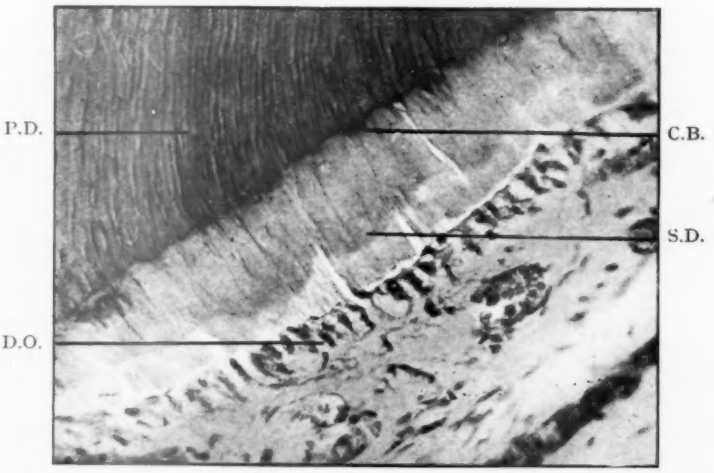

FIG. 4*b*.—× 300. Reaction under silicate cement. Higher magnification of area B, fig. 4. S.D. = Secondary dentine. D.O. = Degenerating odontoblasts. C.B. = Calcific barrier. P.D. = Primary dentine.

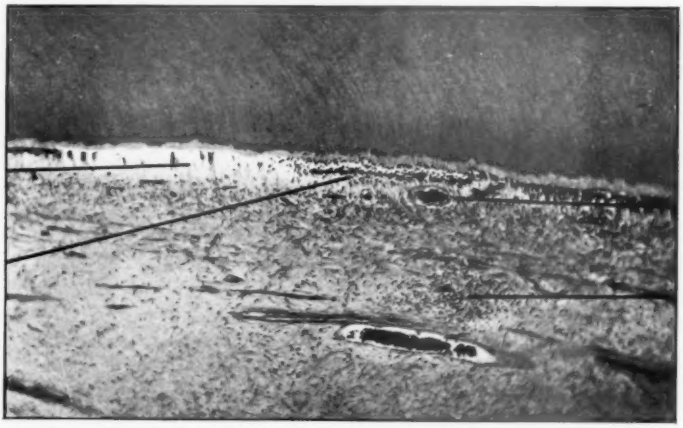

FIG 5.—× 90. Reaction under silicate cement (2 weeks). Girl, aged 12. S. = Damaged odontoblasts due to intercellular congestion of tissue fluid. D.O. = Area of degenerated odontoblasts. R.C. = Round-cell infiltration. C. = Capillary.

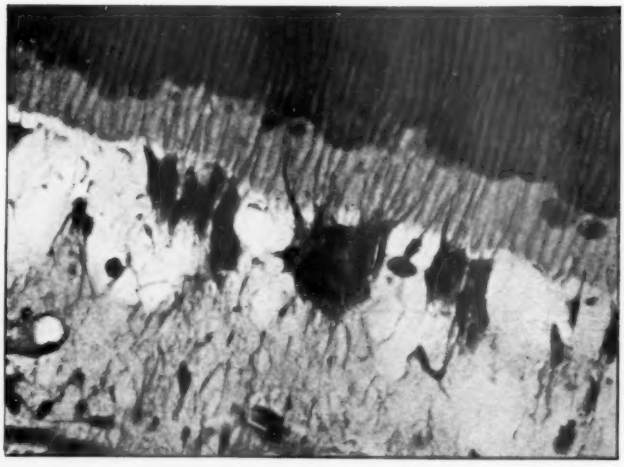

FIG. 5*a*.—× 480. Reaction under silicate cement. High power magnification of area S, fig. 5. Displacement and bunching of odontoblasts due to congestion of tissue fluid.

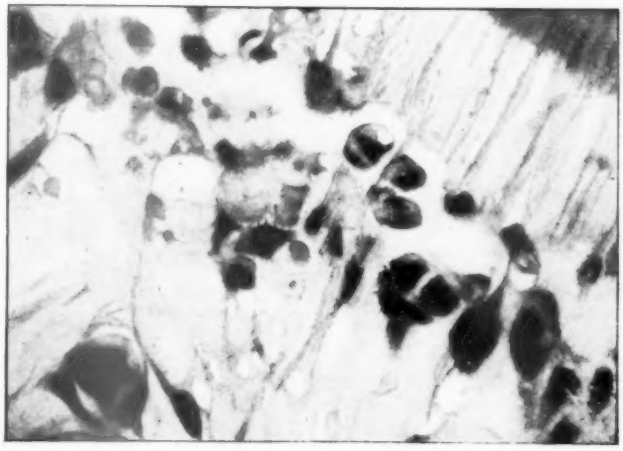

FIG. 5*b*.— × 1,000. Reaction under silicate cement. High magnification of area D.O. fig. 5. Destruction and degeneration of odontoblasts.

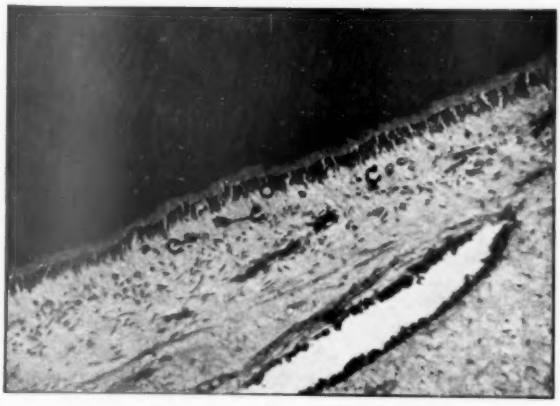

FIG. 6.— × 90. Pulp under cavity filled with zinc oxide and eugenol (4 weeks). Boy, aged 12. O.Z. = Odontogenetic zone. O. = Odontoblasts. C. = Capillaries.

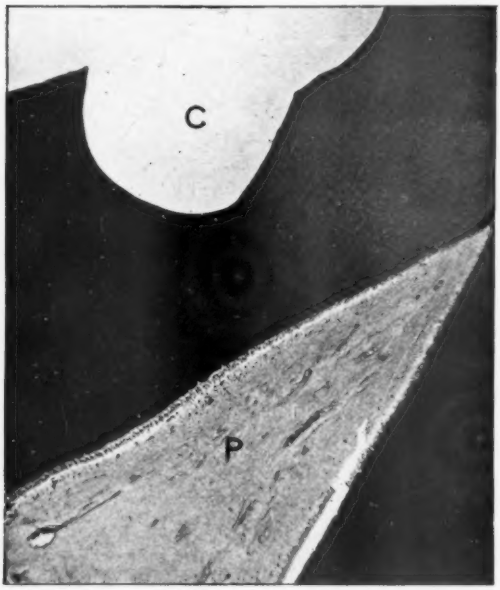

FIG. 7.—× 30. Zinc oxide and eugenol filling (5 weeks). Boy, aged 11. No reaction. C. = Cavity. P. = Pulp.

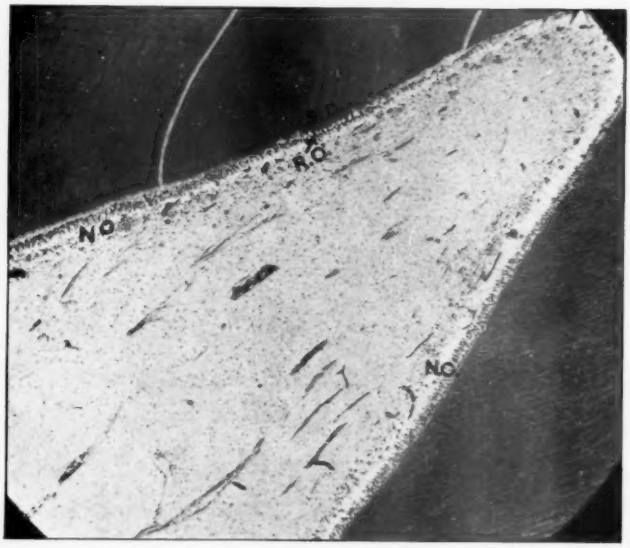

FIG. 8.—× 40. Pulp under cavity filled with zinc oxide and eugenol (9 weeks). Boy, aged 10. Slight reaction. S.D. = Secondary dentine. R.O. = Reduced odontoblasts. N.O. = Normal odontoblasts.

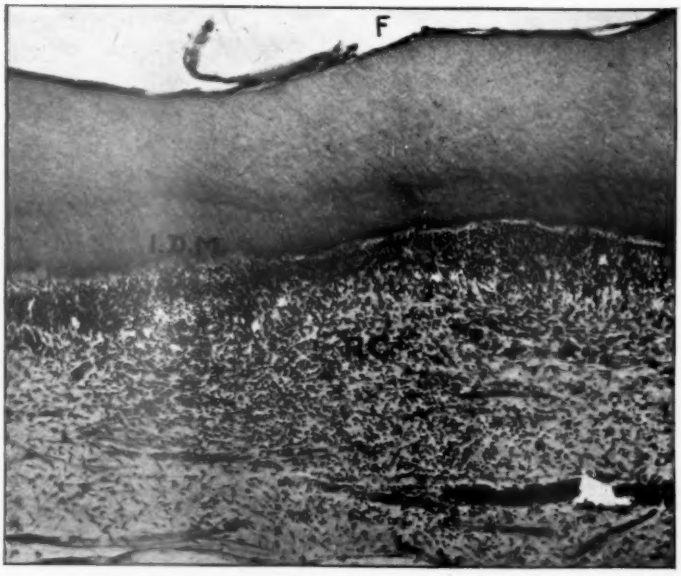

FIG. 9.—× 90. Reaction under copper oxyphosphate cement (3 weeks). Girl, aged 11. F. = Floor of cavity. I.D.M. = Irregular dentine margin. R.C. = Round-cell infiltration.

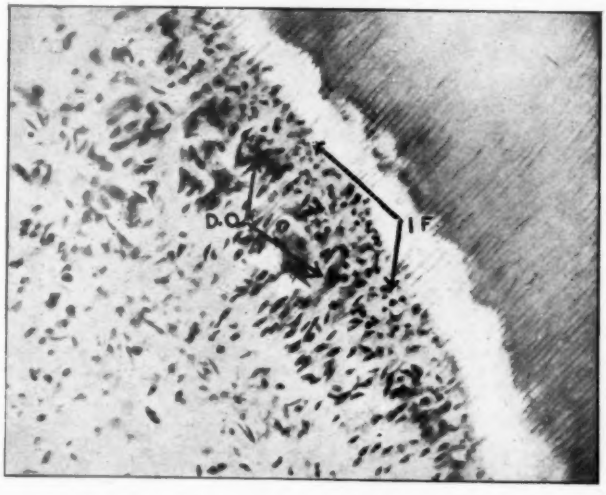

FIG. 9*a*.—× 300. Reaction under copper oxyphosphate cement. I.F. = Inflammatory cells. D.O. = Degenerated odontoblasts.

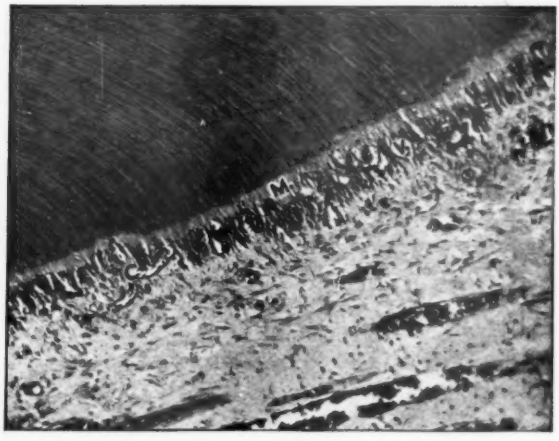

FIG. 10.—×90. Reaction under copper oxyphosphate cement (3 weeks). Boy, aged 12. M. = Matrix. V. = Vacuole. C. = Dilated capillary.

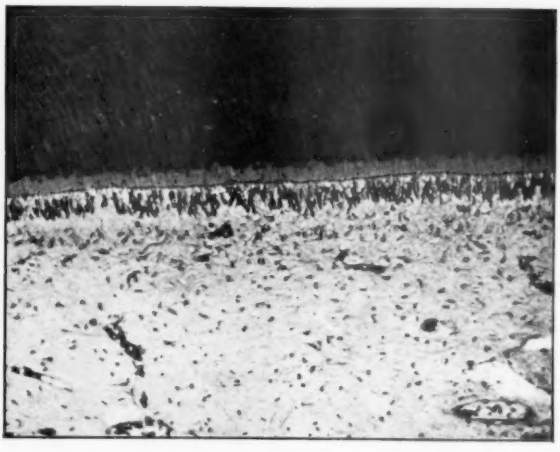

FIG. 10*a*.—× 90. Normal odontoblasts and odontogenetic zone below area shown in fig. 10.

III. *Zinc oxide and eugenol.*—In the experiments where cavities were filled with zinc oxide and eugenol, although slight changes were occasionally observed, no serious reaction took place in the pulp. Fig. 6 shows the area under a cavity four weeks after filling. The odontogenetic zone and odontoblast layer are undisturbed. Some capillaries (C.) have formed underneath the odontoblasts, the rest of the pulp tissue being unaffected. Fig. 7 illustrates a cavity and pulp where no reaction has taken place five weeks after filling. A slight reaction occurred under the deepest part of a cavity nine weeks after filling (fig. 8). At this point a small amount of secondary dentine matrix (S.D.) has been deposited, the odontoblast cells are altered in appearance and are reduced in number. Elsewhere the pulp tissue is normal in appearance. This should be compared with fig. 4, the reaction under silicate cement in a premolar on the opposite side of the same mouth.

IV. *Copper oxyphosphate cement.*—A very severe reaction is seen to have taken place under a deep cavity three weeks after filling with copper oxyphosphate cement (fig. 9). Diffuse round-cell infiltration (R.C.) has occurred, the inflammatory cells extending right up to the dentine margin (I.D.M.) which has become irregular in outline. The odontoblasts under the deepest part of the cavity have been completely destroyed, and the blood-vessels are dilated and hyperæmic. A photomicrograph of higher magnification under a less deep part of the cavity (fig. 9*a*) shows the inflammatory cells (I.F.) close up against the dentine margin, with damaged and degenerated odontoblasts (D.O.) underneath.

The reaction under a shallow cavity three weeks after filling is shown in fig. 10. There is an attempt to lay down new matrix (M.) which is irregular in formation and contains many vacuoles (V.) The odontoblast layer is greatly altered in appearance, many cells have been destroyed and others show degenerative changes. Above a dilated capillary (C.) is a damaged area where no matrix is being formed. For purposes of comparison fig. 10*a* is a photomicrograph showing the normal odontogenetic zone and the odontoblast layer taken below the affected area.

Summary

The results of the preliminary experiments carried out on dogs have been substantially confirmed by this investigation on human teeth.

It has been shown that no serious changes occur in the pulp tissue under cavities filled with zinc oxide and eugenol. In two cases some changes were observed, but the reaction was slight and not of a serious nature. Clinical evidence supports the view that this material is of a non-irritating and sedative character.

Silicate cements are seen to have a marked irritant effect on the pulp, producing degenerative changes two weeks after the insertion of the filling under a shallow cavity. The odontoblast cells undergo various degrees of degeneration or may be completely destroyed. Inflammatory changes in the deeper part of the pulp, evidenced by round-cell infiltration, indicate the toxic nature of this material. These results do not necessarily condemn the use of these cements, but the lining of the cavity with some non-irritating material is clearly indicated. In a plastic state silicate cement will tend to saturate with acid the fluid in the dentinal tubes and after setting this material does not become neutral. In the example shown depth of cavity as a factor influencing the degree of reaction in the pulp is well illustrated. Under the deepest part of the cavity, where the irritant is most intense, degeneration and destruction take place. At the edge, where the cavity floor is further away from the pulp, the irritant has become sufficiently weakened and stimulation of the cells occurs with the result that secondary dentine is laid down.

Silver amalgam produces a definite reaction which presents distinctive characteristics. Vascular changes in and around the odontoblast layer are the most pronounced feature in the early stages of this reaction. With one exception, which occurred under a large and deep cavity, no toxic effect producing round-cell infiltration was seen to occur. The thermal conductivity of this material must be taken into account. In the human tooth subsequent thermal changes will transmit stimuli to the pulp and will thus maintain a degree of irritation which in a deeper and larger cavity will tend to produce a more serious type of reaction with inflammatory changes. For this reason a cavity lining of a non-irritating and non-conducting material is always advisable to ensure proper insulation.

The copper oxyphosphate cement used in these experiments, as in the case of dogs, is seen to be capable of producing a most serious and destructive reaction which, under a deep cavity, extends well into the pulp tissue. The possibility of bacterial infection having occurred accidentally during cavity preparation was eliminated by staining sections in the series with Gram. The results proved to be negative. Generally speaking, copper

oxyphosphate cements have never been suspected of causing pulp irritation, but Crowell (1927) in an investigation into the physical chemistry of dental cements has shown that on the basis of acidity copper cement should be quite as likely to cause pulp trouble as silicates. He states that copper cement is no more acid than silicates to start with, but after several days it begins to become more acid. Further investigation into this group of cements is being carried out.

In conclusion there remains yet one other factor to be taken into account, but which cannot be estimated, namely the degree of vitality of the individual pulp. As the late Dr. Kronfeld has stated: "In every tissue reaction the resistance of the cells is a decisive influence and, since the limit of this resistance is unknown, it is impossible to determine how much irritation is necessary to produce a certain form of tissue reaction." This, in conjunction with the fact that pulps may die without producing clinical symptoms, thereby lulling us into a state of false security, emphasizes the need for further investigation into the pathological changes which may occur as a result of operative procedures carried out in conservative dentistry.

I have to express my thanks to Colonel C. H. Howkins, Acting Professor of Dental Surgery, for his encouragement and for making the continuance of this work possible by placing all the facilities of the Dental Research Department at my disposal, and to Mr. A. W. Wellings for his many helpful suggestions. I wish to thank Mr. E. B. Brain for the making of the lantern slides and his work in colour photography. I am indebted to my wife for the preparation of the sections and for her valuable assistance in the production of the photomicrographs.

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Mr. Manley's paper was discussed by the PRESIDENT, Mr. A. W. WELLINGS, Dr. E. W. FISH, Professor H. F. HUMPHREYS, and Mr. F. N. DOUBLEDAY.

A CINEMATOGRAPH FILM was shown by MRS. SHIRLEY HUGHES entitled "THE DEVELOPMENT OF RODENT TEETH."

Section of Proctology

President—W. B. GABRIEL, M.S.

[*June* 11, 1941]

DISCUSSION ON FACTORS WHICH MAKE FOR SAFETY IN THE PRE-OPERATIVE AND POST-OPERATIVE TREATMENT OF CARCINOMA OF THE RECTUM

Mr. E. R. Flint: The material on which my remarks are founded consists of 86 cases of carcinoma of the rectum operated on in seven years. In the cases under review, when excision has been performed, Kraske's method has been employed in all, as it is safer than the combined method and the ultimate results are just as good.

These 86 cases have all had colostomy, practically all of the left inguinal type, with a mortality of 3·4%. In 49 excision has followed after an interval of from two to three weeks with an immediate mortality of 8%; that is to say I have deemed 56% of the growths removable—the only factors prohibiting excision, apart from obvious secondary deposits, have been fixation to the lateral pelvic walls, and definite involvement of the base of the bladder or urethra.

The special risks in operating by Kraske's method are shock and infection of the wound and also cystitis in men. The general condition of patients with carcinoma of the rectum is not particularly poor, and improves appreciably after colostomy. In those cases which appear to be unusually bad risks pre-operative building-up can be accomplished by a good nourishing diet and plenty of fluids after colostomy, aided by glucose, sometimes by continuous intravenous drip therapy and invariably by blood transfusion on the day before operation. Transfusion is particularly called for, because there is likely to be a good deal more bleeding at the time of operation than is the case in most other comparable major procedures.

Provided the growth is freed without perforation the real risk of infecting the wound arises when the gut is cut across; this is accomplished in exactly the same way as when the duodenum is cut when performing gastrectomy, that is to say by severing it between Payr's clamps, cauterizing the cut end, and infolding it with a running suture of Pagenstecker's thread—the greatest care being exercised to protect the cut end from coming into contact with the wound at any point.

To make doubly sure that infection shall be controlled I always insert—before closing the wound—a three-way Carrel's tube through the upper end of the incision. One tube lies in the hollow of the sacrum and the other two in the crevices on each side at the pelvic wall; they are stitched in position to prevent escape from the selected sites. These tubes are flushed out with Dakin's solution two-hourly for the next week or so. In addition gauze soaked in the same fluid is lightly laid against the whole raw surface and removed on the second day. A large rubber tube is placed in the deepest part of the cavity and removed on the fourth or fifth day. Possibly sulphonamide, powdered over the whole raw surface, might be as efficient but I have not yet tried it.

This technique has been successful in preventing infection.

Retention of urine, especially in men, is common after Kraske's excision, and a very troublesome cystitis often follows. I always put the patient on continuous bladder washing from the time he gets back to bed, as advocated by Mr. Cuthbert Dukes. This

is kept going for several days and helps to prevent cystitis and to improve the outlook for these patients.

In order not to injure the urethra a large gum elastic bougie is tied in at the beginning of the operation and removed at the end. Operative details and the question of recurrence do not come in the scope of this discussion; there is one point, however, which affects the patient's comfort, that is the treatment of the intestinal stump. I prefer to infold it and drop it into the wound rather than stitch it to the skin leaving a mucus-secreting sinus. Generally the wound eventually heals completely, and there is no subsequent trouble with the blind end. Occasionally a sinus forms, but the patient is no worse off than he would be had the gut been brought to the surface in the first place.

Surgeon Rear-Admiral Gordon-Taylor: For the successful extirpation of a cancerous rectum perhaps the most important pre-operative measure is the pre-operative decision as to the type of surgical procedure to be adopted in the particular case. Precious minutes will not then be wasted, and unnecessary manipulations and repeated turning of the patient will be avoided.

The surgery of malignant disease is the surgery of the lymphatic system. The only thorough and really radical operation for a carcinomatous rectum, the only ideal cancer operation based upon a sound knowledge of lymphatic anatomy and pathology, is some type of combined operation, whether the abdomino-perineal method of Ernest Miles, or the operation undertaken in the reverse direction, the "perineo-abdominal" operation.

Although some form of combined operation may be the only truly radical operation for a cancerous rectum, nevertheless for a considerable proportion of cases and in the hands of a large percentage of surgeons, a radical operation of the magnitude of an abdomino-perineal or a perineo-abdominal extirpation may be quite beyond the powers of the patient's recovery.

The relative percentage of cases of cancer of the rectum to which the radical or some "makeshift" operation is applicable will vary with the condition of the patient and with the skill and the experience of the surgeon. A super-surgeon will attain success where the less skilled or less experienced courts failure; thus an obvious pre-operative factor in determining success is the choice of a surgeon of *experience*, of *skill* and especially of *judgment*.

In forming a judicial estimate of his patient, the surgeon will consider the age, sex, and nationality; the blood picture, the cardiovascular, pulmonary, urinary and nervous systems all demand study. The bodily configuration of the patient is of no little moment; the existence of diabetes or Bright's disease, a history of gout, syphilis or recurrent phlebitis will influence the surgeon in his choice of operation. Some rely upon the Moots-McKesson test of operability—marked deviation from the pulse-pressure ratio percentage loads the scales against the patient in any operation of magnitude.

Is it possible to convert the "noli me tangere" for whom no operative removal can be considered or at any rate for whom the most thorough radical extirpation cannot be contemplated into a patient who is a "justifiable risk" for some type of rectal excision? Age itself is no absolute barrier to successful radical surgery; all surgeons of experience can count septuagenarians amongst their successful abdomino-perineal resections; yet age must impose her decree upon surgical enthusiasm. The blood picture can be improved by transfusion. The defective cardiovascular system may be improved so as to enable the patient to survive at least a perineal excision.

The prostatic may require per-urethral diathermy resection, or even a suprapubic drainage. Such patients, however, can never be serious candidates for a combined radical operation.

Fat is a terrible handicap for the surgeon and a menace to the prognosis, and where the extent of the growth permits of some delay, measures may be instituted to reduce the weight of the patient. A preliminary biopsy is of value.

Of all pre-operative measures determining the success of a rectal extirpation, none is more important than *preliminary drainage of the bowel*. This may often be adequately secured by the internal administration of magnesium sulphate and the employment of enemata; in other cases operative drainage of the bowel is required in the form of a colostomy or a cæcostomy. Loss of fluid resulting from the employment of watery purges or from a cæcostomy is easily and accurately compensated by the institution of a "*drip-infusion*" *of a glucose-saline solution*. This is a most valuable measure of safety.

I have no experience of the pre-operative employment of the sulphonamides in cases

of cancer of the rectum. These are probably best employed locally in the perineal wound and in the abdominal incision *at the time of the operation*. There is ample experimental evidence and some clinical proof of their value when employed in this manner.

That surgeon will prove the most safe and successful who neglects no pre-operative measure to "make the patient safe for surgery", and who employs the appropriate operation for the particular case under consideration. The surgeon may still be of good heart despite indications that the patient is unlikely to stand a combined operation; for the perineal operation is associated with a low mortality in competent hands and in the ampullary variety is followed by the prolongation of life for many years. Furthermore, the Hartmann operation carries fewer risks than the combined procedure, and is well worth performing for new growths in the pelvic rectum; moreover before such a patient there dangles the hope of a continent sphincter.

Dr. Cuthbert Dukes: My function is to describe the help which a pathologist can give in the co-operative enterprise of curing a patient of cancer of the rectum.

In diagnosis.—For many years it has been the practice at St. Mark's Hospital to carry out a routine biopsy examination before operation in all cases of cancer of the rectum. This simple and harmless procedure, though not always essential for diagnosis, often provides information with regard to the grade of malignancy and the distinction between columnar and squamous-cell carcinoma.

In assessing fitness for operation.—Of chief importance in this respect is the recognition of anæmia and defective renal function. Treatment of anæmia certainly deserves a place in the list of factors which make for safety. Investigation of renal function is of particular importance in men who may suffer from prostatic obstruction, but it often provides useful information in other cases also. The estimation of the blood urea is all that is required as a rule.

In supervision of blood transfusion.—It is one of the functions of the pathologist to supervise the grouping of patients and prospective donors. At St. Mark's Hospital a few c.c. of blood is collected from each patient a few days before excision of the rectum. The serum is separated and stored in the refrigerator and is used for a direct matching test between the recipient's serum and the donor's red cells. In relation to blood transfusion also the aim should be to give just as much blood as the patient has lost. To obtain accurate data I estimated the blood lost in ten successive operations of perineo-abdominal excision of the rectum. The average was 500 c.c., the range being from 100 to 1,000 c.c. After discussing each of these cases with the operating surgeon I formed the impression that an experienced surgeon generally knows fairly accurately how much blood has been lost at operation, so that there is no need to make the laborious estimation of blood loss a routine procedure. But it is useful to keep in mind that most patients lose about 500 c.c. of blood.

In the elucidation of any complications which occur during convalescence.—After operation it is most important that anything going wrong should be recognized early and diagnosed correctly, and here the pathologist may often be of assistance. There are four tests which should always be undertaken immediately there is any sign of serious complications during convalescence from rectal cancer. Two of these are tests on the blood and two on the urine. The blood tests are—first, a complete blood-count to detect unsuspected anæmia or severe leucocytosis, and secondly, a chemical analysis of the blood, particularly of the blood urea. I recently carried out a series of biochemical tests to watch over the convalescence of ten successive cases of rectal cancer, estimating each day the hæmoglobin, blood urea, blood chlorides and alkali reserve. These and other similar investigations have convinced me that in all cases of paralytic ileus or renal failure the first blood test which will show anything wrong is a rise of the blood urea. In the course of a few hours this may ascend rapidly from the normal level of 20 to 40 mgm. to over 100 mgm. In paralytic ileus this rise in the blood urea precedes by several hours any alteration in the level of the blood chlorides or alkali reserve.

The two urine tests which I also regard as indispensable are a bacteriological examination to detect infection and a test for the excretion of chlorides. Urinary infections often begin with severe constitutional symptoms and can only be recognized by microscopical and bacteriological tests. This is well known, but I shall describe a test whose value is not so widely recognized, namely, the estimation of chlorides in the urine. In cases of paralytic ileus a deficiency of blood chlorides ultimately occurs as the result of loss through vomiting or gastric distension. As already mentioned, this is preceded and accompanied first by a

rise in the blood urea and later perhaps by a decline in the alkali reserve, but the earliest sign of all may be a deficient excretion of chlorides in the urine. This can be recognized by the simple qualitative test with silver nitrate which shows whether chlorides are present in normal quantities or are considerably diminished or absent altogether. The other tests which I have mentioned—the blood-count, estimation of blood urea, microscopic and bacteriological examination of the urine—require special apparatus and training, but the estimation of urinary chlorides is no more difficult than the tests for albumin and sugar. It would be a factor making for safety in the post-operative treatment of carcinoma of the rectum if tests for urinary chlorides were carried out as a routine for the first few critical days after the operation of excision of the rectum.

Detection of chlorides in urine.—Add to half an inch column of urine ten drops of concentrated nitric acid and half an inch column of 3% silver nitrate.

When chlorides are present in normal amount a heavy curd-like precipitate of silver chlorides appears at once. When chlorides are slightly diminished the solution appears milky or opalescent. When absent there is no turbidity.

The nitric acid is added to prevent precipitation of urates and silver phosphate. The silver nitrate solution need not be exact.

A control test should be carried out with a normal urine. If the tubes are allowed to stand for a few minutes the size of the flocculent deposit provides a rough measurement of the quantity of chlorides present.

Mr. Naunton Morgan (*in absentia*—read by Mr. Lloyd-Davies): *Post-operative treatment.*—There can be no doubt, since the water and electrolytic balance of the surgically-sick patient has received more attention, that convalescence is smoother, abdominal distension less and the mortality rate lowered, after severe abdominal operations. Both pre- and post-operative control of fluid balance is essential.

The body normally loses from the kidneys, skin (insensible water loss and sweat), lungs and fæces about 2,500 to 3,000 c.c. of fluid in twenty-four hours. Further, the reasonable average requirement of sodium chloride is about 5 g., which is represented by 600 c.c. of normal saline. The *basic ration* is therefore 3,000 c.c. of water containing 5 g. of sodium chloride.

During and after a major operation, there is a greater loss due to increased sweating, respiratory exchange and blood loss. In the first twenty-four hours it is therefore necessary to give an additional 500 to 1,000 c.c. of fluid. The *basic ration* during the twenty-four hours following the operation is therefore about 3,500 to 4,000 c.c. of fluid.

When complications occur, such as vomiting, distension, fever, diarrhœa, &c., a *supplementary ration* must be given in addition to the *basic* allowance, to cover this abnormal loss.

Since normally the gastro-intestinal tract secretes and reabsorbs between 7,000 and 10,000 c.c. of fluid per day, it is in the abdominal cases that great abnormal loss is most common. With intestinal obstruction and distension, a large amount of both fluid and electrolytes may thus be lost by vomiting or by passage into the lumen of the intestine or its wall. Abnormal loss of gastro-intestinal contents must be made good by the administration of both fluid and electrolytes. Normal saline more or less covers this loss.

Though the best way of giving fluid is by the mouth, the administration of fluids by this route after extensive abdominal operations may be dangerous. It has been shown by many observers, and recently by Douglas and Mann, that peritoneal irritation will produce reflex intestinal atonicity and distension. As the result of operative trauma and localized or generalized infection, temporary paresis of the gut occurs. Those who listen daily to abdomens after laparotomy will confirm this by the slumbering silence of the alimentary tract for one or more days after operation. To pour fluid into these slightly distended and poorly contracting coils of intestine is unsound. It is therefore necessary to give fluids parenterally or rectally. After combined excision of the rectum, fluids and electrolytes should be given by the intravenous route.

Plasma protein and electrolytes maintain the osmotic equilibrium and blood volume, but the water in which they are dissolved is not available for the excretion of metabolites. It is therefore essential to give water which will be free to act as a vehicle of metabolic interchange. For intravenous use, such water may be given as isotonic 5% dextrose in distilled water because the sugar will be oxidized, leaving the water as a free agent.

The body requires its 3,000 c.c. of water per day but only 5 g. of NaCl. This sodium chloride can be given as 600 c.c. of normal saline and the remainder of the daily ration

of water as 2,400 c.c. of 5% dextrose in distilled water. The two solutions may be ready mixed and an isotonic solution containing 4% dextrose, 0·18% NaCl in distilled water is obtained. This balanced fluid recommended by Avery Jones and myself some years ago will prevent the excessive administration of normal saline with its dangers of hydræmia and œdema and has proved very satisfactory.

When distension or vomiting occurs, additional normal saline is required. The amount of vomit is measured and a similar amount of normal NaCl given. If distended coils of intestine retain fluid and electrolytes, a further estimated amount (600-1,000 c.c.) of normal saline is necessary. Excessive sweating and diarrhœa are likewise balanced.

The use of the Ryle or Miller-Abbott tube for the treatment of vomiting, and distension as the result of paralytic ileus, peritonitis or dynamic obstruction is an essential part of post-operative care. The removal of toxic bowel contents and their replacement by an equal volume of intravenous normal saline is imperative.

The anxiety experienced by many surgeons to get the patients' bowels open by cruel stimulation of both the patient and his tired intestine, apart perhaps from the giving of the physiological acetylcholine, is wrong until gut contractions are definitely audible through a stethoscope, or wind is passed from the colon. The use of morphia for the comfort of the patient is important, for though morphia is said to stimulate the gut, its effect is cumulative. There are of course rare cases of idiosyncrasy to morphia.

The time for gentle stimulation of the intestine has arrived only when it emits its awakening tinkles of movement. Greater activity may now be encouraged by the use of small enemata, supplemented if needs be by an intramuscular injection of prostigmine. After wind or fæces are passed, mild aperients are given for the first time. Following colostomy, large enemata should not be given at first, since retention in the colon may produce kinking of the splenic angle and fatal obstruction supervene. I have seen this, at autopsy, on more than one occasion.

Little mention has been made of the rôle of plasma protein in this brief survey. All are agreed that routine blood transfusion after combined excision of the rectum has reduced the mortality rate. This is partly due to the replacement of plasma protein, lost not only in blood but also from serous oozing from the large raw area in the pelvic cavity during and for some time after operation. Protein loss is normally made good by adequate diet.

There is evidence that plasma protein is lost into the wall of the intestine in intestinal obstruction associated with distension of, and tension within, the small gut (Fine, Hurwitz and Mark, *Annals of Surgery*, **112**, No. 4, 546, October 1940). Apart from surgical shock there appear to be few conclusive investigations of plasma protein in post-operative cases, but it must be remembered that the poorly nourished patient or one who has suffered from prolonged sepsis and inanition may have a low plasma protein. In the presence of hypoproteinæmia there is a danger that administration of moderate amounts of normal saline intravenously may produce œdema. This can occur even with a normal blood chloride. Furthermore, hypoproteinæmia is a probable factor in the delayed healing of wounds (ruptured abdomens, &c.).

In the surgically sick patient, especially when sepsis and distension are present, the plasma albumin and globulin should be estimated and plasma administered accordingly.

Mr. Frankis Evans: In this problem there are three important decisions. First, when to operate; secondly what operation is to be performed; and thirdly under what circumstances is that operation to be done. In all this the anæsthetist is directly concerned, for the choice of anæsthetic, and the method of its employment is dependent upon the condition of the patient, the operation to be done, and whether any therapeutic measure such as the administration of blood is contemplated during the operation.

The anæsthetist should invariably see the patient beforehand, so that he may instil confidence and evaluate the operative risk. It is of the utmost importance that the patient does not see the anæsthetist for the first time at the operation, but should be able to regard him if not as an old friend at any rate as a well-wishing acquaintance. The preliminary examination should include an evaluation of the circulatory system as a whole, and this necessitates the examination of the heart, arteries, pulse-rate, exercise tolerance, and blood-pressure. The respiratory system also must be examined for evidence of infection, and with regard to adequate lung expansion. It is also essential to know the hæmoglobin percentage, and the condition of the excretory system as evidenced by the blood-urea estimation.

I would like to stress the time factor in the operation for cancer of the large bowel

where shock is an unwelcome and ever-present guest, any procedure taking longer than one hour tends to emphasize this fact; therefore the combined perineo-abdominal excision with two surgeons working simultaneously below and above has much to recommend it. The anæsthetist, too, can help very materially in reducing the time of operation and the onset of shock by choosing that form of anæsthesia which will render the surgeon's task as easy as possible. To this end he must use an anæsthetic which will give the greatest degree of abdominal relaxation with the least disturbance to the patient, and which will render the respiratory movements slow and of small amplitude. At the same time the patient must not be poisoned with slowly excreted drugs and noxious vapours. It is my practice, therefore, to give a preliminary injection of omnopon gr. ⅓ with scopolamine gr. $\frac{1}{150}$ subcutaneously, followed by the rapidly excreted barbiturate pentothal g. ½ intravenously. The patient is then given a spinal anæsthetic of heavy percaine 1·6 c.c. in the second or third intervertebral space and the table is tilted to a 5° Trendelenburg position. This gives adequate relaxation and anæsthesia up to the seventh thoracic for some two hours. The patient is kept under by the administration of nitrous oxide and oxygen. With this method the patient comes round quickly and there is least disturbance to his organism as a whole.

The control of the blood-pressure should be in the hands of the anæsthetist, and I would like to stress the two types of blood-pressure fall which may be seen after the administration of a spinal anæsthetic. In the one case the patient remains a good colour, is warm, and has a slow pulse; but if the circulatory system cannot adapt itself to these changed conditions there is a totally different picture: the patient is blue-grey, pinched, and has a rapid thready pulse. It is in this condition that intravenous medication is required. I find that phedracine 0·5 to 1 c.c. intravenously will raise the blood-pressure quickly and adequately, as also will ephedrine by the same route. Neither of these drugs will raise an already fallen blood-pressure if given intramuscularly. This is followed immediately with blood, or saline. This blood drip is continued post-operatively and is followed up with normal saline one part and sterile tap water four parts.

When the patient is back in bed, the foot is raised on six inch blocks, and one pillow is permitted. This is to minimize the risk of headache, it also tends to keep pressure off the pelvic peritoneum. It is better to prevent the patient drinking for twenty-four hours until the gut has begun to move. This obviates sickness by resting the stomach, and the patient gets all the fluid required by means of the intravenous drip. Finally sleep is essential, therefore opium should be given generously.

Dr. Ronald Jarman: Four main points are essential in pre- and post-operative treatment: (1) The condition and comfort of the patient; (2) teamwork; (3) the type of anæsthetic; (4) the immediate after-treatment.

(1) Providing the patient has not got an acute obstruction necessitating a decompression before the main operation, all examinations should be done while the patient is in hospital, such as the condition of his upper respiratory tract, chest, &c., and tests for blood urea and blood sugar, or specimens of urine, &c. I examine the patient at this time, taking blood-pressures before and during the pre-operative treatment.

In the majority of these cases the pulse pressure is either low or high. If low, I have cause for anxiety, but as long as the pulse pressure is high, no matter what the age is, I do not have to worry about the case during the anæsthetic.

I always tell the patient that there are three main factors in his operation: the surgeon, the anæsthetist and himself. He knows that the surgeon will do his part to the best of his ability and likewise the anæsthetist. When that has been done it is up to him to do his job in getting better as quickly as possible. To do this he has to be amenable to the people in charge of him, to his surroundings, and adapt himself to the treatment.

(2) I have worked with two surgeons whose technique is, except for a few small points, the same. They have worked together on a large number of these cases and the operation has been discussed to the last detail.

(3) Here my technique is as follows:

To ensure the patient a good night's rest, medinal gr. 10 and aspirin gr. 10 are given the night before. The Roche ampoule omnopon gr. ⅓ and scopolamine gr. $\frac{1}{150}$ is given one hour before the operation to produce a state of somnolence and pentothal g. ½, that is to say 10 c.c. of 5% solution is given to the patient whilst in bed, and he is therefore unconscious of being moved to the operating theatre.

A spinal anæsthetic, using Etherington Wilson's technique, is given. Ephedrine gr. ½ or gr. 1 is injected whilst the patient is sat up.

In the case of men 14 or 15 c.c. of light percaine, strength 1:1,500 at just over body temperature, is injected into the theca. The patient is kept sitting up for sixty seconds from the commencement of the injection and then put down into 15° Trendelenburg position. In the case of women, 12 or 13 c.c. light percaine is all that is necessary.

The patient is then given nitrous oxide and oxygen by means of a McKesson machine and after further preliminaries such as emptying the bladder, seeing the shoulder rests are in position, the operation is allowed to commence in the fullest Trendelenburg.

It may be necessary, during the operation, for a continuous saline and glucose drip to be given. One has to be prepared to do this by putting a cannula into a vein in either of the legs.

Post-operatively, the anæsthetist should be prepared to have to give whole blood or saline and glucose intravenously.

The patient lies on his back when he returns to his bed, with a clear airway, and as soon as he starts to come round is given a pillow, and after six hours he is put into a full Fowler's position.

I have had 5 deaths on the table out of 500 cases. All these have been over the age of 65. The age-incidence has been from 27 to 77, though actually I have done a case of a young man of 23. Deaths within twenty-four hours have been nil. At forty-eight hours they have been ½%, and deaths following this period have usually been after five or seven days and are 12%.

The success of the operation is no doubt due to the speed at which it has been done. The average time, taking all types of cases, has been one hour and twenty minutes.

Where the patients have partially collapsed on the table their recovery has been dramatic when a pint of whole blood has been given, and usually they have made an uninterrupted recovery.

The following points have to be borne in mind:

(1) The possibility of coronary thrombosis. Two of my immediate deaths at post-mortem examination were due to this, though clinically there was nothing to indicate such a possibility.

(2) The condition of latent chest trouble, usually found in old people, where chest symptoms develop two or three days after the operation.

(3) The increased risk where the patient's resistance is at a very low ebb.

Lt.-Col. J. A. MacFarlane: I shall limit my remarks to one or two considerations—the relief of chronic obstruction and the improvement in the patient's general ability to withstand the particular operation which has been decided on.

Discussion of these measures necessarily includes the question of a choice of operation. The surgeon should not commit himself to a single type of operation. Each patient should be studied according to age, general condition, site of lesion, &c., and the operation chosen which will give him the best chance of survival. In minor degrees of obstruction by growth in the rectum proper, when the patient is a good general risk—not judged on age standards alone—our practice has been to keep him on clear fluids, daily administration of mag. sulph. and colon washouts for six to eight days, and then after 2,000 c.c. of glucose solution and a transfusion of 500 c.c. whole blood on the day preceding, to carry out an abdomino-perineal resection.

If after such preparation the bowel is found to be poorly prepared, even slightly distended and œdematous, we do the operation in two stages after the Labey technique, and during the following fortnight the bowel is washed through with 1:1,000 acriflavine solution in preparation for the resection.

In the eighteen months preceding the war some experience was gained with the Devine operation, and several growths in the lower sigmoid were resected. It is felt that this procedure should be the one of choice in those growths above the peritoneal reflection, yet too low to permit of a Mikulicz resection.

A procedure as radical as the abdomino-perineal can be carried out except for the removal of the ischiorectal fat, and there is no doubt that after thorough washing of the distal loop after a transverse colostomy of the Devine type, an anastomosis of colon to rectum can be done with safety, and the sphincter function saved.

In all cases with acute obstruction from rectal cancer it would seem wise to do a blind cæcostomy. This is a life-saving operation, and will tide the individual over the emergency. The plan of precedure for a radical operation can then be worked out.

In the general examination the residual urine should be estimated—the estimation

of non-protein nitrogen in the blood or other kidney functions test be carried out. If there is evidence of prostate enlargement with much retention, it is wise to deal with this condition by transurethral resection before the attack on the rectal growth.

In cases where the hæmoglobin is reduced below 70, one or two transfusions may be given in preparation. In all cases where a resection is planned a transfusion of 500 c.c. whole blood is given on the evening preceding the operation and 500 c.c. are available to be given during or following the operation if necessary.

Dr. P. L. Mollison: A previous speaker has mentioned the use of plasma in the pre- and post-operative treatment of carcinoma of the rectum. Pre-operatively, transfusion of plasma finds its most correct place in the treatment of obstruction of the small intestine and not of the large, because only in the former can the plasma volume be shown to be reduced. In the treatment of immediate post-operative shock it is more reasonable to use blood, as the hæmoglobin is almost always found to be low in such cases, and the anæmia can thus be corrected at the same time as blood volume is being restored. It should be remembered that plasma at present proves almost three times as expensive to produce as blood, both in donors and in money.

Mr. E. T. C. Milligan: It has become a routine procedure to test the fitness of the patient's body to withstand this operation in the way Dr. Cuthbert Dukes has described, but I also try to discover the patient's own attitude to his disease.

The remedy for fear is trust and knowledge, so the patient must find throughout his illness that all his contacts are trustworthy. The surgeon, his assistants, and the nurses, should foster faith and confidence by their efficiency, knowledge, loyalty, and confident action. The patient's practitioner is invaluable if he himself is knowledgeable and is free from fear.

Some are ashamed or afraid to admit their fears. Some fears are unformed and the patient is inarticulate. All patients are ignorant of or misinformed about this big enterprise so that the resulting fears are unreal and imaginary. It is good practice to explain what the patient needs to know and then to ask about specific fears, but to avoid suggesting fresh ones. To revealed fears the surgeon can give an answer out of his own life and the experiences of other sufferers. The common fears are centred around the anæsthetic, the colostomy, the loss of economic security, interference with social activities and relationships, curability, and the dread of pain and death.

In practice it is found that many false and curious ideas disturb the patient's mind, and he gains much relief by sharing them with his surgeon. Amongst uncommon fears which cause stubborn refusal to face the ordeal is conflict between the patient's religious ideals and the proposed action of the surgeon. A guilty or shameful personal secret, which may be revealed during loss of conscious control, leads to unreasoning refusal. A pension terminating at death is sometimes a concealed dread or impediment because of its effects on dependants.

The ideal conditions for successful surgery are that the patient has implicit faith in his surgeon and his assistants, together with a vital spiritual faith applied and well tried in the commonplaces of life and now exercised in his crisis.

Mr. A. Dickson Wright: I consider the large wound cavity created in the perineum as similar to the recent war wounds in which sulphonamide powder has proved so valuable, and I have made it a routine to sprinkle the wound liberally with this powder and to place pieces of a special gelatine impregnated with 50% sulphonamide in all the corners of the wound. This gelatine slowly dissolves in the wound serum and keeps up the sulphonamide action.

The sulphonamide after absorption into the blood-stream does good work in keeping down post-operative urinary infection.

Section of Physical Medicine

President—JOHN COWAN, M.B.

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The Thermionic Control of Electric Currents in Electro-Medical Work

By P. BAUWENS, M.R.C.S., L.R.C.P.

WHEN one considers the various fields where thermionic valves have been adopted for the control of electric currents on account of their wide range of applicability, it is somewhat surprising that they have not yet made their appearance in electrotherapy except in rectifying and oscillating circuits.

It is interesting to study those properties of valves, which might be exploited, and the advantages which might accrue from their utilization in controlling or modifying the flow of current in direct current circuits. The simplest type of valve is the diode. It consists of two electrodes enclosed in an evacuated space. One of these is heated electrically and is referred to as the cathode. It acts as an emitter of electrons. The other, or anode, is merely a plate or a cylinder in its vicinity. When a diode is connected up to a source of direct current (*see* fig. 1) in such a way that the cold electrode, or anode, is positive in relation to the cathode, a current will flow. Its magnitude will depend on a number of factors, such as the distance between the electrodes and their dimensions. As in other circuits, the current is a function of the E.M.F., but in this case, this relation only holds good within certain limits, for the number of electrons available for the transmission of the current across the gap between cathode and anode is determined by the temperature of the cathode itself. Once all the electrons emitted are being used, further increase in the E.M.F. produces no change in the current and the valve is said to be saturated.

This is well illustrated by the curves shown in fig. 2. The ten curves represent the current values for ten different temperature-states of the cathode. It will be noted that in this particular case as long as the potential difference across the valve is in excess of 50 volts, the current in the circuit is entirely controlled by the temperature of the cathode. In other words, variations of impedance in other components of the circuit will not affect the current value as long as the voltage across the valve does not drop below 50 volts.

The fact that the temperature of the cathode is easy to control by regulating the current heating this electrode, makes such a valve a very effective current regulator. Unfortunately temperature lag in the cathode makes instantaneous adjustment impossible.

When galvanic currents are employed for electrotherapeutic purposes, they are as a rule controlled by means of potentiometers, cell collectors, or resistances, and in such cases the value of the current is greatly influenced by the impedance of the patient, which is all but constant. The changes of resistance in the superficial layers of the skin are so great that they can be measured by means of an ordinary milliampere meter; nor are these of any importance in the application of unmodified galvanism. They do, however, become a source of error when testing muscles and nerves. For every time the active electrode is moved, the value of the current varies, rising at each closure of the circuit until the resistance of the patch of skin immediately under the electrode has broken down and become constant.

This can, of course, be minimized by adequate soaking of the skin, and by having resistances in the circuit of such magnitude as to render these variations of resistance in

the skin negligible. Unfortunately this coarse variation is not the only one to be contended with. One which is undetectable by ordinary methods causes the current to drop very rapidly almost as soon as it is made. It does not result from a change in resistance but from the production of a back E.M.F. developed by the banking up of ions on either

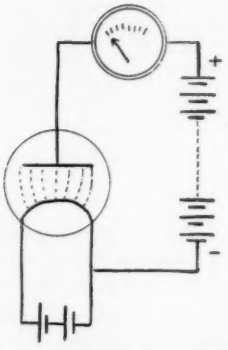

FIG. 1.—Typical circuit incorporating a diode valve.

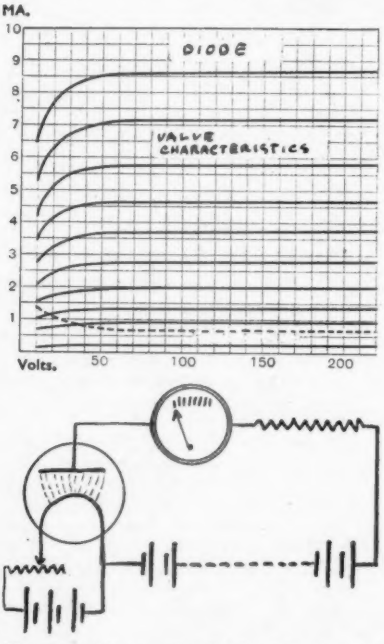

FIG. 2.—Characteristic curves obtained in circuit in which current is regulated by means of a diode. The filament temperature is conveniently controlled by means of a variable resistance in the heater circuit.

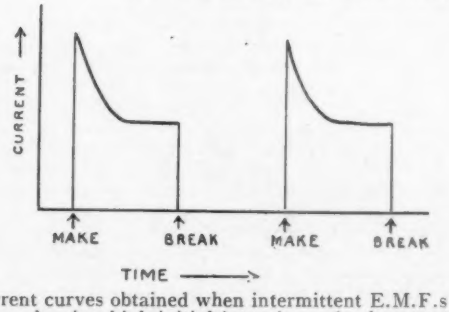

FIG. 3.—Current curves obtained when intermittent E.M.F.s are applied to the body—showing high initial intensity and subsequent decrease.

side of polarizable membranes. An oscillographic study of the current obtained when an interrupted E.M.F. is impressed across a patient shows how the current reaches a high instantaneous value at make, but rapidly drops to a lower one when the back E.M.F. is established (fig. 3).

It must therefore be remembered when muscle testing with apparatus in which the galvanic current is controlled by means of a potentiometer that the response obtained may have been produced either by the high peak of short duration or by the more prolonged current of lower intensity, according to the excitability characteristics of the tissues under test.

In this connexion it is interesting to note that a condenser, which when discharged through a simple resistance gives rise to a true exponential current curve, when discharged through tissues gives rise to a kinked exponential curve owing to the effect just described. The discharge is rapid until the back E.M.F. is developed and is then slowed down (fig. 4). When no precautions are being taken to exclude polarization phenomena at the level of the electrodes, further distortion occurs.

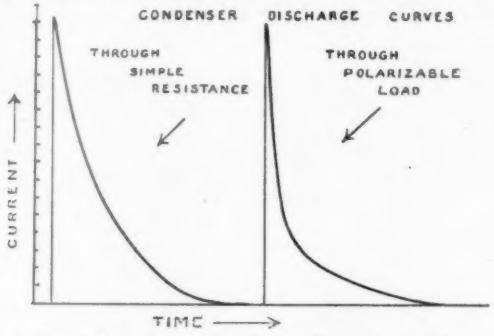

FIG. 4.—Curves of condenser discharges through a simple resistance and through a polarizable load.

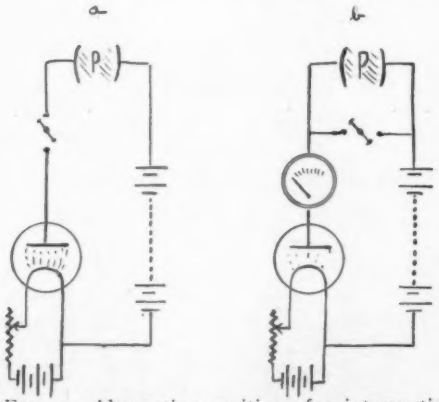

FIG. 5.—Alternative positions for interrupting device in circuits in which current is controlled by means of a diode.

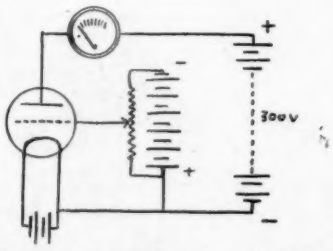

FIG. 6.—Typical triode controlled circuit.

From these considerations it is clear that where a modicum of accuracy is aimed at in the measuring of threshold currents, a method whereby these fluctuations of the flow can be minimized must be employed. This can be achieved by utilizing a saturated diode instead of a potentiometer to limit the current. Two alternative circuits can be employed (fig. 5*a* and *b*).

With a supply of 300 to 350 volts, the diode valve will be saturated under practically all conditions and the current in the circuit will be determined almost entirely by the temperature of the filament. No variations of resistance, back E.M.F. in the tissues or

at the electrodes will materially affect it. For this reason it is possible to make the current through the patient intermittent by shunting the patients' terminals with a short-circuiting device (fig. 5*b*). When the terminals are shorted no current passes through the patient.

If a meter is wired into the circuit as shown in fig. 5*b* it will be observed that the current is exactly the same whether it passes through the short-circuiting device or through the patient. Incidentally the latter arrangement is interesting for it offers a path for the depolarization currents at the moment when the electrodes are short-circuited and shows how easily responses at break are obtained in these circumstances.

Thus, by using a saturated diode valve to control current, errors due to variables are eliminated and measurement of current is greatly facilitated.

It was mentioned that temperature lag of the filament was a drawback. This is entirely because of the annoyance it provokes when regulating the current and not on any other account.

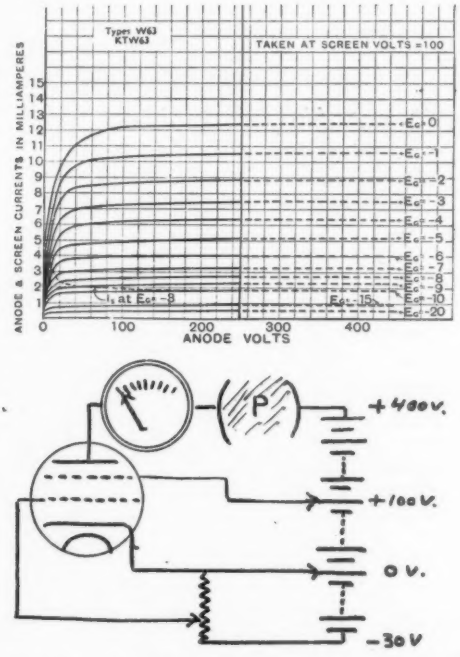

FIG. 7.—In circuits incorporating tetrode valves, variations in anode voltage do not materially affect the current.

In a valve, control of the flow of electrons from cathode to anode can be effected by the introduction of a third electrode between the existing two. This is usually meshed and is called the grid (fig. 6). In this case the potential on the grid determines the number of electrons which pass from anode to cathode. The effect of a negative potential on the grid will be to repel oncoming electrons, thus decreasing the number crossing the space. On account of the closer proximity of the grid to the cathode, it easily neutralizes the influence of the more remote anode, and therefore small changes in the grid potential can bring about important alterations in the current flowing through the valve.

With the simple triode, however, the current is to a great extent influenced by the voltage across the valve and therefore variations in the load impedance affect the current.

To overcome what would constitute a grave disadvantage, yet a fourth electrode is inserted between the grid and the anode. This additional grid is kept at a constant positive potential. The electrons which penetrate the control grid are thus accelerated by a positive potential which is not affected by changes in the load. Fig. 7 represents a circuit containing a tetrode valve. The accompanying curves show how the characteristics of such a circuit approach those of a saturated diode inasmuch as the current value is not greatly influenced by changes in anode voltage.

Great advantages accrue from the fact that with this method of control the current reaches its correct value for a given grid potential instantaneously, instead of with a lag as is the case with the diode. That variations of the grid potential with a tetrode valve working under suitable conditions will faithfully reproduce identical variations in the current, independently of the nature of the load, is a further advantage. For this implies complete control of the current even when the load is as variable and inconstant as in the case of tissues.

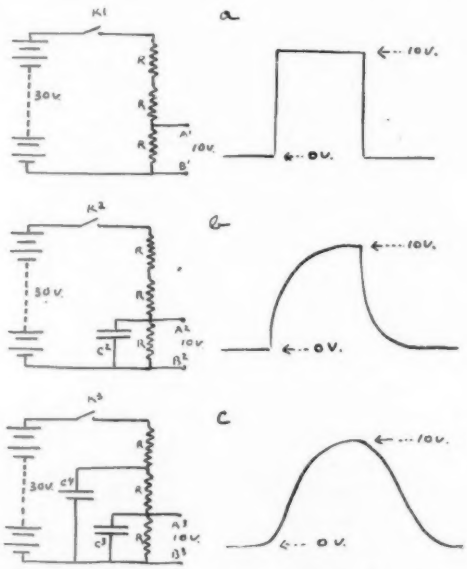

FIG. 8.—E.M.F. curves obtained in circuits incorporating various arrangements of resistances and capacities.

By means of resistances, condensers, inductances and with the aid of valves, it is possible to produce almost any shape of E.M.F. wave form—the simplest being the rectangular wave. Such a wave-form is obtained when a current is made and broken in a circuit without capacity or inductance. In fig. 8*a*, if these provisos are adhered to, the potential difference across A^1—B^1 will reach a value of ten volts instantaneously, and drop back to zero when the key K^1 is depressed and released. If, as in fig. 8*b*, the points A^2 B^2 are shunted by means of a condenser C^2 at make, the potential difference across points A^2 B^2 is reached after a delay the duration of which depends on the capacity of the condenser. At break, the condenser discharges through the resistance and the potential across it decreases according to the exponential curve which characterizes condenser discharges through non-inductive resistances.

A more symmetrical curve can be obtained by using two condensers, C^3 and C^4, as is shown in fig. 8*c*. The steepness of the gradient at make and break is a function of the capacity of the condensers and the values of the resistances employed. Supposing we wished to pass a current affecting such a wave-form through the body, it is clear that the

direct supply from A^3 B^3 would alter the shape of the wave. This source of distortion may be avoided by applying the appropriate E.M.F. to the grid of a tetrode valve and by including the patient in the anode circuit. By using a potentiometer P instead of a simple resistance R the magnitude of the current can be regulated. In fig. 9, which is the wiring diagram of a workable circuit, a bias battery is included in the grid circuit so that a negative potential of sufficient value to cut off the current through the valve is applied to the grid when the key K is open. This is an elementary form of the apparatus for the stimulation of paralysed muscles to the exclusion of normal muscles by means of progressive currents.

With the switches in the position shown in the diagram (fig. 9) there is no potential difference across the potentiometer P but thanks to the bias battery the grid of the valve is 30 volts negative relatively to the cathode. This would completely cut off the current through the valve. When the key K is closed a current flows through the series of resistances R.R.P. and as these are of the same value the voltage drop across each one will be 30 volts.

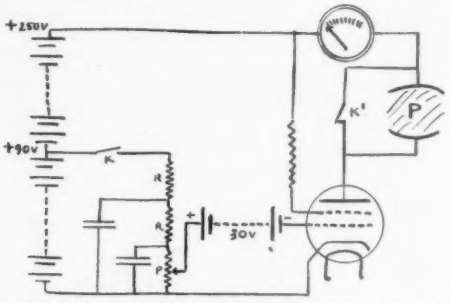

FIG. 9.—Simplified circuit diagram of apparatus for production of progressive currents.

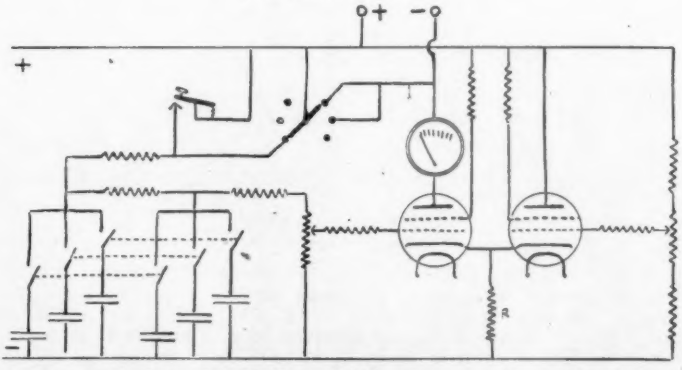

FIG. 10.—Complete circuit diagram of apparatus for production of progressive currents incorporating by-pass valve and switch gear.

When this occurs, the potentiometer slider becomes positive to an extent depending on its position. This potential difference decreases the negative bias on the grid. The anode current resulting from this is measured by the meter. When the two condensers are put into the circuit the current can be seen to reach the same value, but after a delay. When the switch K^1 which short-circuits the patient is opened, the same current with the same wave-form can be observed to flow. This means that the current can be measured or pre-set without its flowing through the patient; an advantage which is not as manifest in this apparatus as in the one to be described later.

As a rule it is not possible to obtain a direct current supply, nor is it expedient to employ bias batteries. Rectified alternating current is resorted to. But the output voltage of rectifiers is affected by variations in the output. To solve these problems, the circuit has to be modified in such a way as to keep the current drained from the rectifier constant. By using two identical valves with a common resistance R, in the cathode lead, and connected up as shown in fig. 10, not only is the current taken from the rectifier of constant value, but the drop of potential across the common cathode resistance R, provides the requisite negative bias on the grid of the valve in the patient's circuit, thus eliminating the necessity of a grid bias battery.

So far, only the control of wave-form and intensity of current have been considered. The control of the duration of flow, particularly when this is of short duration, is of great importance where measurements of muscle and nerve excitability are concerned. For purposes where impulses of short duration are required, condenser discharges have been almost universally used. More rarely rheotomes have been employed. As pointed out earlier, the former do not deliver currents with the anticipated exponential wave-form when the load is polarizable, nor do the latter produce rectangular current waves under similar conditions. Rectangular waves can be obtained by using two triode valves. Fig. 11 shows how the two valves V^1 and V^2 are connected up for this purpose. The anodes

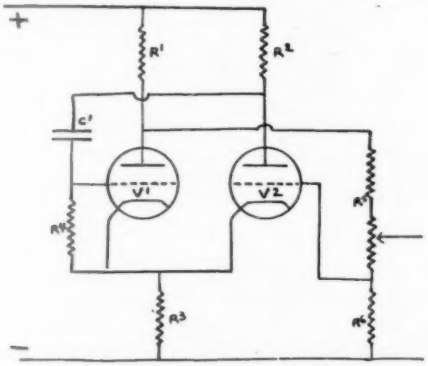

FIG. 11.—Circuit for production of rectangular waves.

have separate anode resistances, R^1 and R^2, but there is a common cathode resistance R^3. Under conditions of rest the valve V^1 is passing current because its grid is connected by way of resistance R^4 to the cathode and has therefore the same potential. This means that through R_1 there flows a current which is the sum of the current flowing through valve V^1 and that flowing through resistances R^5 and R^6 along which a potential difference is developed. The values of R^6 and R^3 are such that in such circumstances the current passing through these two parallel paths causes the grid of valve V^2 to be sufficiently negative to cut off the current through valve V^2.

As no current passes through resistance R^2 there is no drop of potential across this and its lower end is virtually at the same potential as the positive supply.

To trigger off a rectangular wave the grid of valve V^1 is made strongly negative for a very small fraction of a second. This results in an instantaneous cut-off of the electron stream across the valve V^1, leaving no parallel path for the current through R^5 and R^6, Consequently the current through these resistances increases, thus augmenting the potential difference across them. The increased potential across R^6 makes the grid of valve V^2 less negative and this results in a flow of current through this valve, and a drop of potential across its anode resistance R^2, the valve end becoming negative. This sudden negative state is transmitted by displacement through condenser C^1 to the grid of valve V^1, thus taking control of the grid potential of this valve and keeping it negative.

The time during which valve V^1 remains in the cut-off condition will depend on the value of resistance R^4 through which the negative charge on the condenser and grid will leak away. The instantaneous return to the original state is due to "avalanche effect".

As soon as the grid of valve V^1 is no longer sufficiently negative completely to cut off the electron stream, a minimal current flows through the valve—this opens the alternative path for the current through R^5 and R^6, decreasing the current through these resistances and causing the grid of V^2 to become more negative on account of the lessened potential difference across R^6. This in its turn causes a decrease in the electronic flow through V^2 and the lower end of resistance R^2 becomes less negative, which state is immediately transmitted to the grid of V^1, further increasing the current through V^1. This goes on until all the current flows through V^1 and none through V^2.

Although this process has taken some time to describe, the return to resting condition is so rapid as to be virtually instantaneous. A rectangular current wave-form is the result.

The negative impulse of short duration necessary to trigger off the wave is conveniently obtained by using an auxiliary circuit (fig. 12), in which a condenser C^2 is slowly charged

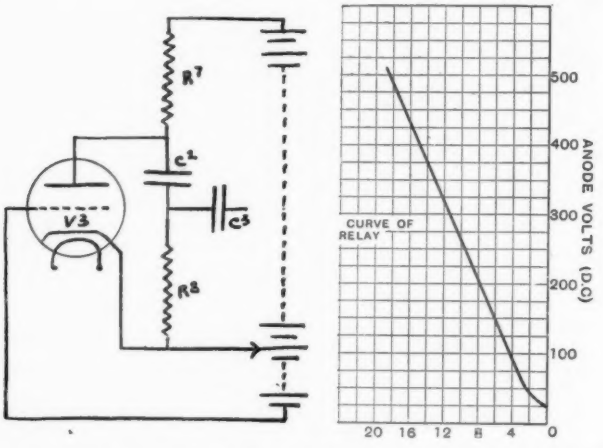

FIG. 12.—Curve showing relation of striking voltage to grid voltage in gas-filled relay utilized in trigger circuit such as shown in diagram.

through a resistance R^7 until the potential across its plates reaches the break-down voltage of an argon gas-filled relay V^3 and then discharges. Such a valve differs from the ordinary triode in that it passes no current until a critical voltage, depending on the grid potential, is impressed across its anode and cathode when it suddenly allows current to flow until the condenser is almost discharged.

During the discharging of the condenser there is a difference of potential across the resistance R^8. It is the resultant negative state which is transmitted to the grid of the valve in the next stage. To make this an impulse of very short duration a condenser C^3 of very low capacity is interposed.

In the wiring diagram of the complete apparatus for producing currents of rectangular waves (fig. 13) and which I use for the assessment of muscle and nerve excitability, the different circuits described can be recognized in spite of some additional components.

In the gas-filled relay (V^3) circuit a selector switch, S^1, enables one of four sets of condensers and resistances of different values to be charged and discharged. Each combination has its own time-constant. With a combination consisting of a large capacity condenser and large resistance, single impulses with a period of rest are obtained, whereas with small capacities coupled with small resistances, rapidly repeated impulses are produced, resulting in a tetanizing effect.

This circuit further contains an electronic tuning indicator, V^4—better known in wireless apparatus as a "magic eye". Here it indicates the time and frequency of the impulses.

In the wave-form-producing circuit the two triode valves are replaced by a double

triode, V^1 V^2. This is a valve in which the electrodes of a triode are duplicated V^1 and V^2. The duration of the impulses is regulated by varying the resistance R^1 in the grid circuit of the controlling valve V^1. It is expedient to utilize a resistance in twelve steps, one for very long impulses for the measurement of the rheobase and eleven for impulses of varying shorter durations for the estimation of chronaxy.

A thirteenth position of the selector switch makes the grid strongly negative and therefore gives rise to a constant instead of an intermittent current in the output circuit.

In the output circuit two tetrode valves with a common cathode resistance are used. One, V^5, is included in the patient's circuit, the other, V^6, functions merely as current by-pass. As pointed out before, with valves wired up in this way the total current is constant. When the grid biasing of the by-pass valve V^6 is correctly adjusted, this valve passes all the current and none passes through the valve V^5 in the patient's circuit until a positive impulse reaches the grid of this valve. This valve, V^5, will then pass a current which will depend on the setting of the intensity controlling potentiometer P, and the ballast valve, V^6, will pass that amount less.

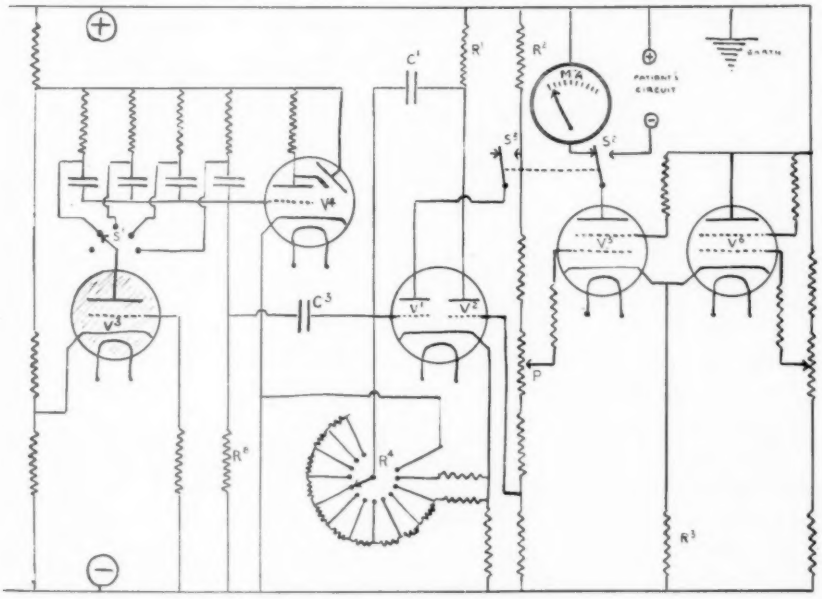

FIG. 13.—Wiring diagram of apparatus for measurement of muscle and nerve excitability by means of rectangular waves.

The action of the double-pole two-way switch S^2 S^3 is easy to follow. When in the position shown in the diagram, the anode current of the valve, V^5, passes through the milliammeter. This current is determined by the position of the potentiometer P.

When the switch is thrown over to its other position, the current through the potentiometer P decreases because it is now shunted by valve V^1 which by-passes some current. Only when valve V^1 ceases to pass current as the result of a negative impulse on its grid from the previous stage does the current through the potentiometer P momentarily resume its high value. While the current through the potentiometer P is of low value, the potential difference across it is not sufficient to raise the grid potential of valve V^5 above cut-off potential, therefore whatever the position of the slider, no current will pass through the patient. But the instant valve V^1 has its flow of electrons cut off, the current through the potentiometer P increases for the duration of the cut-off, and the grid of

valve V^5 will rise above cut-off potential and allow a current to pass through valve V^5 and through the patient, of the same value as the current which was read on the meter when the switch was in the original position.

Such a machine is simple to use since no special electrodes need to be employed. It is, however, essential to have the same area of electrode in contact with the skin, and in the same position for the measurement of the rheobase and the chronaxy. The reason for this is that no matter how small or how large the area of electrode in contact with the patient is, the same amount of current will be passed through that area. Clearly this will affect the density very much when changes in area of contact occur. To ensure constancy of this contact area I employ a simple curved electrode (fig. 14), the head of which

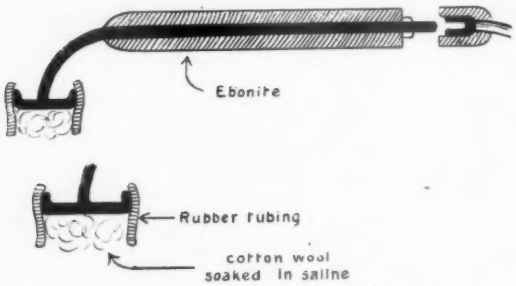

FIG. 14.—Interchangeable electrode for muscle and nerve testing.

consists of rubber tubing plugged with cotton-wool soaked in saline. This moulds itself well to irregular surfaces, such as intermetacarpal spaces in a subject with wasted hands.

It is essential when constructing such a machine for the measurement of tissue excitability, to earth the positive side of the electrical supply.

In a subsequent discussion Dr. Cooksey said that he hoped that an effort would be made to standardize the apparatus by expressing the various durations in milliseconds.

By means of a cathode ray oscillograph Dr. Bauwens demonstrated how the intensity and the duration of flow of the current could be regulated quite independently. He also showed with the aid of a phantom load that the current and the rectangular wave-form remained unaffected by wide variations in the resistance of the load.

Section of Ophthalmology

President—A. J. BALLANTYNE, M.D.

[*June* 20, 1941]

The Treatment of War Injuries of the Eye

By T. M. TYRRELL, F.R.C.S.

IN the ten months that have elapsed since the beginning of heavy air attacks on London I have learnt that our peacetime methods of treatment of eye injuries do not apply very well to wartime.

Some of the cases I have been able to deal with at once. Others have had to wait because I was unable to be in two places at once. It was this latter fact that first brought home to me the possibility of leaving a badly injured eye for twenty-four hours, and still get a good result. In several cases I found that it was easier to deal with cases that had had to wait, and consequently I soon began to leave patients unoperated on purpose, and I found that the results were apparently better. In the past I have been impressed by the degree of shock and restlessness shown by patients with perforating eye injuries, and the need for getting a good 7th nerve block in these cases before submitting the eye to a thorough examination or operation.

I think that after the lapse of time this shock passes off, and the patient is in a better condition to stand operation. This must apply with even more force in the case of air-raid casualties, who are even more shocked than civilian cases of injuries to the eye, as they have often been concussed, buried or have suffered other injuries.

You will have been struck by the extraordinary grimy condition of most of these unfortunate people. The dirt appears to have been blown deep into the pores of the skin, and the conjunctival sacs are usually filled with a slimy mud-pie made up of mucus and dirt. It is well to subject all these eyes to two or three hourly irrigations with an alkaline lotion before attempting any operative interference, and at the time of operation I like to irrigate the conjunctival sac with 2% silver nitrate for long enough to produce a slight film of white over the corneal surface, before commencing the operation. This forms a protective coat over the particles which may be embedded in the cornea or conjunctiva, and helps to prevent infection.

WAR INJURIES TO THE EYE

I. *Non-penetrating.*—(*a*) Dust and debris in conjunctival sac; (*b*) glass in conjunctival sac; (*c*) concussion injuries of globe.

II. *Penetrating but not perforating.*—(*a*) Wounds of lids; (*b*) corneal foreign bodies; (*c*) burns of cornea, lids and conjunctiva; (*d*) glass in cornea; (*e*) glass in sclera; (*f*) subconjunctival metal or dust or other foreign matter.

III. *Perforating injuries.*—(*a*) Metal; (*b*) glass; (*c*) other matter. (i) Of cornea, uncomplicated; (ii) of cornea, complicated; (iii) of corneo-scleral junction; (iv) of sclera.

I. In the *non-penetrating injuries* there is little to be added to what I have said about group (*a*). All glass must, of course, be removed from the conjunctival sac, and it will usually have to be picked out. Glass is the most tenacious of all the conjunctival foreign bodies. Concussion injuries of the eye may be divided into: (*a*) Hyphæma; (*b*) torn iris; (*c*) torn lens capsule; (*d*) dislocated lens; (*e*) vitreous hæmorrhage; (*f*) detached retina; (*g*) commotio retinæ.

I have seen large numbers of these cases, and the accepted treatments are well known; but I would particularly refer to traumatic detachment, of which I have seen not more than one or two. I have had not more than ten detachments which have come to the various out-patient departments that I attend, since the bombing started, and of those not more than half have been air-raid casualties at the alleged time of onset of the detachment. Those who had had a detachment as the result of a direct blow on the eye were just as rare, and I think that this is the general experience. Owing to my position in the heart of London I have had to send all my detachments away to base hospitals, and I have no record as yet of the results obtained, but I understand that there have been quite good results on unpromising material.

II. *Penetrating but not perforating injuries.*—*Wounds of lids* are fairly common, and by far the most difficult to treat. Nearly all go septic unless the wound edges are excised, and with the lid there is not much left to excise when there is a big gash in the tissues. So far I have contented myself with cleaning the edges of the wound with peroxide of hydrogen and cutting out all obviously damaged tissue unlikely to survive; and when in any doubt I have not sewn up the edges. The most difficult are those with a damaged tarsal plate. The correct treatment here would probably be a complete tarsectomy, but I have not tried it yet.

When there are multiple corneal foreign bodies, I do not touch them. These patients are soon comfortable if the eyes are kept well dilated with oily atropine ½% b.d. and later with paroleine drops, and the foreign bodies rapidly fall out. Any which are left can be picked out later. Mr. Savin has pointed out that a great help in removing corneal foreign bodies of this class is a Leitz binocular operating microscope, such as may be found in most zoology laboratories, for the dissection of our smaller fauna.

Burns.—Most people agree on the danger of using tannic acid for skin burns. The violet dyes have given good results. Burns of the cornea are very uncommon. You will have read Jules Verne's books in your youth, and will remember one in which the hero has his eyes put out with red hot irons, and owing to the film of tears over the cornea, which was turned into steam, he found when he recovered that the cornea had not been burned at all. I had an example of this not so long ago. A small boy aged 11 accidentally ran a stream of molten lead into his eye. When I saw him I was able to pick out a complete cast of the conjunctival sac, and beneath it was the cornea, quite clear and bright, though the conjunctiva of the fornices was œdematous and parboiled. He got away with nothing worse than a small symblepharon of the lower fornix.

The other groups are dealt with in much the same way as the corneal foreign bodies, but I had one case with subconjunctival dust ingrained, in which I had to excise the whole area of the conjunctiva affected, together with the lump of dust before the eye would heal.

III. *Perforating injuries.*—After the evacuation from Dunkirk I had a case of a soldier with a wound of the sclera at the outer side of the left eye, with the tip of a large foreign body peeping through the sclera on the nasal side, having passed right across the vitreous but failing to penetrate the sclera on its way out. Having failed to extract it with a giant magnet, I seized it with a fixation forceps and eased it out; there was no gush of vitreous or pus but as the injury had been sustained some days before a fibrinous exudate round the foreign body had probably prevented the vitreous from escaping.

In the other case a piece of metal had passed across the bridge of the nose, through the lower fornix of the sclera of the left eye to lodge in the left zygoma. The eye had to be removed eventually.

In a similar case in which the foreign body was protruding on the temporal side of

the sclera, and the lens was undamaged, I tried to extract it with a pair of fixation forceps, but owing to the shocked and restless state of the patient I had to desist. On the third day the foreign body fell out, and the wound shut up like an oyster. He has now $\frac{6}{18}$ vision, and a strand of retinitis proliferans which looks like leading to a detachment of the retina.

In another case a bomb fragment entered an eye from which a cataract had been successfully extracted some years previously. I left him alone except for putting him on a mydriatic. After a week I tried to pull it out with a pair of fixation forceps but I found I had got hold of a protruding knuckle of choroid. The choroid fortunately did not rupture, and within three weeks the gap had closed up and the man had $\frac{6}{12}$ vision. There was never any sign of inflammation. Perhaps this is the result of having no lens matter to set up a post-operative iritis.

Glass has been the chief bugbear in these perforating injuries. It is very difficult to see even with the slit-lamp, and even more difficult to extract. Fortunately in most of the cases the glass has worked its way out even from the depths of the wound. In one case, a girl had a wound of the sclera which had apparently closed, but at the end of ten days a piece of glass ½ cm. in length and about 1 mm. in breadth extruded from it, pricked her lid and came out quite easily when pulled with forceps. The eye now shows a strand of retinitis proliferans in the vitreous which appears to be subsiding.

Most glass injuries are so liberally peppered with small glass fragments all over their upper parts, that any attempt to X-ray them for the purpose of an intra-ocular glass fragment is lost in the cloud of other small pieces of glass. How should we treat those cases who have a piece of glass lodged in the eye which shows no tendency to come out? Do they get any foreign body reaction, and do they require operative interference? I think the only indication for operative interference would be interference with the vision in an otherwise useful eye.

I have had about 20 to 25 severe glass injuries, and have had to remove ten eyes which were too pulped to save. The majority of the others were cases in which the glass had perforated the cornea or sclera and fallen out again, and all that was necessary was a clean up, iridectomy, and conjunctival flap. I have had one or two illuminating cases. One was admitted during an all-night raid, with some 80 casualties, mostly to one ward, and there was naturally some confusion as to the identity of the injuries sustained by any particular patient. This man was very badly shocked, and was receiving a plasma infusion when I visited the hospital next morning. He had his head swathed in bandages, and I was told that both his eyes had been pulped and had been removed by the surgeon. Consequently I did not examine him in his bad condition, but gave instructions to take the bandages down that night and irrigate both sockets. The Sister did so, and found the left eye badly pulped, and the right eye with a wound through the lid and the cornea above the pupil, with a prolapse of iris filling the wound. The next day I found that the iris was neatly blocking a small wound of the cornea. As the man was still exceedingly ill, I decided to leave him till more favourable cases had been dealt with. The next day the wound in the right eye had closed still further, though the iris was still up to the back of the wound. I do not know whether one is in danger of getting sympathetic ophthalmia in cases where there is a wound of both eyes, but I began to feel that there was little harm in waiting to see with this case, and indeed patience has been amply rewarded. The right eye had also a wound of the lens, and now the lens matter has absorbed, and the man awaits a final needling on a quiet eye. The left eye is now quiet, somewhat shrunken, with no perception of light.

The only other intra-ocular foreign body of interest I have seen was in a policeman who was wounded by an explosive incendiary bomb, and was admitted with a pulped right eye in which a large foreign body had been treated by X-ray. As the injury was a recent one, and as the eye was not savable I removed the globe. On cutting it open I found a large piece of brick, which had been driven straight through the cornea.

Conclusions

I. Glass injuries are the chief bugbear of air raids. To prevent them we need a vigorous campaign to inform the general public of the dangers of flying glass, and to

prevent shopkeepers from replacing broken windows with yet more glass. Firemen and fire watchers should have a protective visor to keep flying debris out of the eyes.

II. Operative interference is not quite such a necessity in these cases as I have always been taught. All the cases that had to be left twenty-four hours before operation did quite well, despite the danger of infection. It may be that I have been very lucky so far, in having had so little infection.

III. A magnet is not usually necessary for these cases. Most of the foreign bodies of the metallic class are large and they either damage the eye so extensively that it has to be removed, or they go right through the eye into the orbit, or stick in the sclera on the way out.

Discussion.—Mr. HAROLD RIDLEY said that eye injuries caused by aid raids were most serious, for not only were both eyes frequently involved but the injuries were more frequently complicated than in civil cases. Intra-ocular hæmorrhage was usual and when that cleared commotio retinæ, macular degeneration or retinal detachment were frequently revealed.

Intra-ocular foreign bodies were frequently non-magnetic. In one case a non-magnetic foreign body, probably aluminium alloy, was seen at times freely suspended in the vitreous, and this eye eventually suffered from progressive macular disease. Magnetic foreign bodies were frequently round or square as opposed to the flake of metal almost invariably found in industrial accidents. When these clumsy fragments perforated the sclera it was generally easier to remove them via the wound of entry rather than by the usual anterior route. If detachment were visible or suspected a diathermy barrage could be applied around the wound.

Though multiple corneal foreign bodies caused intense lacrimation and photophobia it was difficult to remove them all at once and several sessions were usually required to deal with those particles causing marked irritation or inflammation of the cornea. Some deeply embedded fragments caused little or no reaction and were better left alone if the track epithelialized over.

Glass wounds were common, especially from broken windows. Glass was always difficult to see in an eye but window glass was relatively opaque to X-rays and a useful hint for approximate localization was to X-ray the eye from front and side after fitting a Zeiss contact glass. The relative position of the shadows gave a good idea of the position of the foreign body.

Mr. AFFLECK GREEVES said that he agreed with Mr. Tyrrell that it was advisable to deal with certain cases after a lapse of time, when the patient's general condition had improved. With regard to glass, all the intra-ocular glass cases he had seen, due to injuries sustained in air raids, had had the eye disorganized. He had not seen any cases with small bodies in the eye; the foreign bodies had all been large. He could cite one instance—not a war case—in which a piece of glass was left in the eye and did no harm. The injury was caused by the explosion of a bottle. One eye was completely disorganized and the other was penetrated by a small piece of glass which lodged in the back of the eye. The lens became opaque. He evacuated the lens, and the eye remained perfectly quiet, the resulting vision being $\frac{6}{5}$. The eye never gave any further trouble although the glass was still there. He asked if Mr. Tyrrell had seen cases in which a piece of glass had been embedded deeply in the cornea, and if so, had it an irritating effect? He had seen one case in which a triangular piece of glass was deeply embedded in the centre of the cornea. The eye in this case was otherwise damaged, and it was impossible to see the foreign body until the eye had settled down. The piece of glass became surrounded by an area of slight haze, and it seemed to him that this opacity was increasing. He therefore took out the glass, although rather loth to do so as it was so deeply embedded that it was impossible to avoid a certain amount of trauma. The case was too recent for him to say whether the haze was going to clear up or not. Had any member had a similar experience?

He suggested that the haze might have been caused by inbibition of fluid through the torn fibres of the substantia propria of the cornea.

Mr. C. DEE SHAPLAND agreed that glass injuries were the commonest as the result of bombing, and also the most difficult to deal with. Spicules of glass in the anterior chamber could quite easily be removed through a keratome section in the usual position, followed by an A.C. washout, and recently he had been able to free a particle of glass deep in the cornea and projecting behind the posterior corneal surface, by introducing an iris repositor through a keratome section followed by A.C. lavage. Glass in the vitreous was best left alone. He agreed with Mr. Tyrrell that no harm ensued from

leaving perforating injuries for some twelve to twenty-four hours, by which time the patient had a chance to get over the state of primary shock, the injury to the eye being almost invariably associated with multiple traumata to other parts, usually of the face, of greater or lesser severity.

Dr. W. G. DAVIDSON said that he had had two cases which were due to explosions. The cornea in both cases was opaque, and it seemed a hopeless task to remove all the small particles which were embedded in the eye. In the first case he treated it by lavage and atropine and it took a long time to clean up. In the other case he took the bolder step of removing the whole of the corneal epithelium and the result was an almost perfectly clear cornea. Here were two cases which looked the same but the case treated on conservative lines gave a much less satisfactory result than the other.

Mr. Tyrrell had mentioned the fact that molten metal which went into the eye had not burned the cornea. He himself had seen a case in which molten metal went right into the eye, but he had only to pick a cast of metal off the cornea, the epithelium being perfectly intact. The explanation was probably the phenomenon of the spheroidal state of water. When a drop of boiling water was dropped on to red hot metal it passed into the spheroidal state. The drop ceased to boil. Indeed evaporation was so rapid that the loss of heat lowered the temperature of the drop instantly to 206° F. A similar phenomenon might occur when the cornea was brought into contact with extreme heat such as molten lead, the moisture in the eye at once assuming the spheroidal state and giving protection by a layer of vapour. It was well known that the hand could be passed into molten lead without injury, and there was thus a scientific foundation for the story of Michael Strogoff, whose eyes were undamaged in spite of an attempt to burn them out.

He had been using albucid for about nine months in every case in which, in a war injury, there was any evidence of sepsis. He had used it in perforating wounds of the cornea and had been surprised at the rapidity with which they cleared up. He used it on a punctured wound of the cornea, where the case was not seen until four days after the occurrence, and had a good deal of discharge with pus in the anterior chamber. This again cleared up perfectly. He had also used it in children afflicted with blepharitis and conjunctivitis and the results were very good. A 30% solution was useful in infected wounds of the eyelids. On application the condition healed by first intention.

Mr. VICTOR PURVIS said that he had seen several cases in which small splinters of glass were lying on the iris and causing no trouble whatever. If within the cornea, again, they did not cause trouble unless they were near the surface, and the epithelium over them became abraded, when the eye immediately became irritable and then the foreign body had to be removed.

Mr. Tyrrell's suggestion of 2% silver nitrate as an irrigation fluid was rather a strong solution and 1 :1,000 silver nitrate had proved very generally successful. It would for example make an intra-ocular operation quite safe in the presence of a pneumococcal culture.

No speaker had as yet mentioned blast injuries causing vitreous hæmorrhage. Had any member seen a definite case of eye injury due to blast when nothing, apparently, had hit the eye, other than an impact of air?

Dr. DOROTHY CAMPBELL (in reply to the last speaker) said that she had seen three cases in which evidently some expansion of the atmosphere had split the choroid. This generally occurred as a clear split in the choroid, a thin crack, semicircular, about as long as the disc, and situated between the disc and the macula. She had seen another case of sudden proptosis due to retrobulbar hæmorrhage, in which blindness occurred immediately. There were no changes in the retina, and no history other than of exposure to blast.

Mr. J. D. M. CARDELL said that with regard to multiple foreign bodies in the cornea, Mr. Savin was trying an electrolytic method of getting rid of them. He was assisted at Horton by a chemist who selected the electrolyte suitable for the foreign body embedded in the cornea. Other ways in which foreign bodies could be removed included the American method of mounting a very small dental bur in an ordinary trephine and burring each foreign body. In that way the corneal tissue around it was loosened, and thus the foreign body was enabled to come out more easily. Another method was to touch each with carbolic acid. There was a French method of localization which consisted in injecting an opaque substance such as lipiodol as close as possible to the cornea. With lipiodol the X-ray photograph would indicate clearly the curvature of the globe of the eye and the rest of the curve could be reconstructed geometrically

so as to show whether the foreign body was inside or outside the eye. Mr. Ridley's suggestion about putting on a contact glass was helpful, and it might be an additional advantage to place a dot of sealing wax on the contact lens, marking the centre of the cornea of the patient before the X-ray picture was taken.

Wing-Commander KEITH LYLE said that Mr. Tyrrell had mentioned the difficulty of doing operations under local anæsthesia. This could be easily overcome by employing general anæsthesia preferably by the use of intravenous sodium pentothal. As a routine in the Royal Air Force one carried out operations in that way. The cases concerned were usually young men who were sensitive and apprehensive, and one obtained better results without having to rely upon the co-operation of the patient.

He had a case of an intra-ocular foreign body in an air-gunner, who was shot, and had multiple foreign bodies in the face and in one of his hands. The surgeon removed the foreign substance from the hand, and the speaker tested it and found it non-magnetic, so he assumed that the foreign body in the eye was also non-magnetic. This seemed to be so often the case with metallic intra-ocular foreign bodies.

With regard to pieces of glass in the eye, he had a case under observation at the moment in which the injury occurred eight months ago. The piece of glass situated just behind the iris appeared to be causing no trouble and the eye was quiescent. It seemed likely that a piece of glass embedded in the eye was not necessarily a cause of irritation.

Colonel FRANK JULER said that one speaker had mentioned in rather glowing terms the value of albucid as a preventive of sepsis or as a treatment of sepsis when established. He rather doubted whether the application of sulphanilamide as a local measure in the eye had proved generally to be of much value in relation to sepsis.

Squadron Leader A. G. CROSS said that two of the speakers had mentioned blast injuries. He saw an interesting case at about the time of the Dunkirk evacuation. The injury was apparently due to the blast of an exploding bomb or shell; this occurred close to the man, but there was no sign of perforating injury caused by flying metal. Nevertheless, both globes were ruptured. The man was not seen until he came back to this country four or five days after the injury, when the picture was the two ruptured globes and no other wound, and nothing could be done but evisceration of the remnants of the eyes.

With regard to non-magnetic foreign bodies, he felt that when the eye was put up to the magnet one could never be sure that the foreign body, though magnetic, would come forward. In certain cases, a foreign body was clearly seen in the fundus. In one such case that he had in mind, the foreign body might have been embedded in the sclera very firmly, though it did not appear to be, but there was absolutely no reaction to the magnet. There was, however, good vision in the eye, and it was decided that it would be better to do nothing for the time being. About two months later, there was quite definite evidence of siderosis. It appeared that although these metallic foreign bodies might be non-magnetic or so weakly magnetic that they could not be attracted forward, there was sufficient iron in them to cause a siderotic reaction in the globe. During the last war the opinion was formed that to remove non-magnetic foreign bodies by a posterior route did not give very good results.

Mr. S. S. SUMNER drew attention to a method of localization of foreign bodies which might be more extensively practised when the more exact methods of radiological localization were not obtainable. If the position of the foreign body be "roughly" localized by radiography one should reflect the conjunctiva and if necessary a muscle over the approximate position of the foreign body in the eye and then in a dark room, after dark adaptation apply a transilluminating lamp to the cornea so that the light shines into the eye; it (the eye) then lights up like a little chinese lantern. If the foreign body is in the sclera, as most are, its position is marked by a little black dot in the "chinese lantern" of the illuminated bulb. This probably affords more exact localization than is obtainable by other methods.

Obviously it is only applicable to opaque foreign bodies which are situated in the anterior two-thirds or so of the eye but in suitably selected cases is helpful.

Once found the position of the foreign body can be marked on the sclera by a nick with a Graefe knife.

The PRESIDENT said that war injuries of the eye were not very different from civilian injuries, at least in a district like his, where they were very familiar with industrial injuries caused by metal or glass or other foreign bodies, and the treatment was very much on the same lines. There was, however, a larger proportion of serious bilateral

injuries in the war. Certainly among the cases seen in Glasgow there had been a number of these bilateral or binocular injuries which had raised difficult points in treatment. The lesson to be learned there was to hold one's hand in the early stages. He could quote several cases in which both eyes were so badly damaged that it was difficult to say which was the worse. In one case the eye which in the early stages looked the more serious turned out in the long run to be the more useful eye of the two. The one eye contained a large vitreous hæmorrhage, but looked well, while in the other there was laceration of the cornea, iris and lens, and it seemed doomed to removal. Yet this second eye was restored to usefulness while the other never got out of the stage of poor light perception and poor field. One should hesitate about removal of either eye in a bilateral injury until the ultimate result became a little clearer.

It seemed impossible to generalize about glass injuries, for instance as to whether the presence of a foreign body consisting of glass was likely to be fatal to the eye. The question of sepsis had to be considered, also the question of the chemical composition of the glass itself, which might produce a chemical effect on the tissues of the eye, comparable with that of metal in its capacity to destroy vision. If the glass were superficially situated—that is, if it were in the cornea—it could be seen generally by focal illumination, and even if in the anterior chamber it could, as a rule, be removed. Probably it was easier to remove glass from the cornea than to remove metal. Little spicules of metal were very apt to be barbed, and sometimes were difficult to remove without dissection, but glass foreign bodies would usually slip out of their pocket more easily than a piece of metal of comparable size and shape. But if the glass foreign body were in the vitreous or interior of the eye one could do nothing with it and must take one's chance—he did not think it wise to remove the eye because the glass was there.

With regard to multiple foreign bodies, where the slit-lamp showed particles of all sizes, and at all depths from the epithelial surface right down to the posterior surface of the cornea, it was impossible to remove all these foreign bodies by any method. Many such cases were seen in civil occupations, as, for example, during work employing compressed air; in which the workman may receive a gust of compressed air on his face, carrying with it into the eye a large number of small foreign bodies. One could only remove those which lent themselves to removal superficially, leaving the others to take their chance. A good deal had been done in the removal by means of forceps, of intra-ocular foreign bodies which were non-magnetic or non-metallic; but he understood that the prognosis in such cases, even where the removal was successful, was fairly bad from the point of view of survival of vision.

In his own, not very great, experience he had seen during the present war a smaller proportion of magnetic foreign bodies and a larger proportion of non-magnetic foreign bodies than previously. Indeed, he thought he had not had one case of intra-ocular foreign body caused by magnetic metal among the war casualties he had so far seen. One or two were caused by particles of non-magnetic alloys.

The question of the demand for excision of the eye was always difficult, and it would be interesting to hear the general experience with regard to the frequency of excision demanded in war injuries. Out of some 30 serious injuries of the eye received in his hospital eight had required excision—that was, roughly, the proportion found locally.

An interesting point had been raised in connexion with blast or windage injuries to the eye. A number of strange occurrences had been noted, such as intra-ocular hæmorrhage which appeared to be purely the result of air concussion. In civil life injuries to the orbital region resulting from a blow or a fall not infrequently involved damage to the optic nerve, and to the vision, with ultimate optic atrophy. In these there were superficial signs of local injury; but among the eye injuries seen in this war he recalled two cases—both in women—in which there was very little superficial bruising of the brow, not more on the affected side than on the other, but with inactive pupil, immediate loss of vision in the affected eye, and all the signs of optic atrophy. He could not persuade himself that there had been a sufficient blow on the side of the blind eye to account for the injury to the optic nerve. Yet it was difficult to think that concussion by air was sufficient to cause that injury. Those in a position to see these injuries might keep in mind the point as to the possible effects of air concussion. He was sure that some of them escaped detection altogether. In any clinic where the cases were seen in the first place by a physician or surgeon, and there was no external sign of injury to the eye, the ophthalmic surgeon might not be called in consultation, and the lesion would escape notice.

Mr. TYRRELL (in reply) said that he had had only one case of glass stuck in the cornea; it was quiet for two days, and then the glass started to work out. There were

two pieces of glass, pyramidal in shape, and the straight edges were in the centre of the cornea. All one could do was to put a needle underneath them, and they came out quite easily.

No speaker had enlightened them on the point whether, if both eyes were injured, there was any danger of " sympathetic " or not.

He once tried to do some experiments with pentothal, and found the great difficulty to be in controlling the eye. He rather liked to have the co-operation of the patient, though in such a feeling it might be that he was influenced by the consideration that not only should he know what he was doing, but that the patient should know also!

Section of Psychiatry

President—C. P. SYMONDS, M.D.

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Metabolic Investigations in Periodic Catatonia

By S. W. HARDWICK, M.D., M.R.C.P., D.P.M.
(*West Park Hospital*)
and
A. B. STOKES, M.A., B.M., M.R.C.P., D.P.M.
(*The Maudsley Hospital*)

Dr. Stokes

INTRODUCTION

METABOLIC investigations in the field of schizophrenia have been singularly disappointing in their results. This may be attributed to the fact that the total schizophrenic material is far from homogeneous, and the individual schizophrenic patient shows considerable variation in mental state and physical functioning over a period of time; therefore tests carried out on a group of patients on a single occasion are not likely to give consistent findings.

Gjessing's approach has been different from that of others. He has selected a small field in the vast territory of schizophrenia where the case material has shown constancy in respect to many dramatic qualities, and he has followed these single cases through many months with daily biochemical and physiological investigations. The selected patients conform diagnostically to the group called periodic catatonia, and in them he has been concerned with the broad aspects of metabolism in relation to the changing phase of mental state.

In periodic catatonia there are repeated attacks of stupor or excitement the form of which is relatively constant for the individual patient. The attacks come on suddenly and disappear rapidly, while in the intervals the mental state approximates to normal. The attacks have typical schizophrenic qualities and the intervals show evidence of impairment of mental faculties, indicative of schizophrenia, with lack of volition, poverty of ideation, lack of critical ability, emotional flattening and mannerisms.

In association with this periodic change of mental state Gjessing has found a phasic variation in total nitrogen balance and a phasic variation in autonomic function. The variations in all the functions examined occur synchronously, and where the autonomic is under consideration they indicate a swing from one state of vegetative tone to another. Such cases are thus called synchronous-syntonic to distinguish them from others in which the phasic nature of the mental disturbances and physiological functions are blurred, asynchronous and asyntonic. Furthermore, among the synchronous-syntonic cases the phasic nitrogen change is related to the disturbed mental state in two differing ways. In A type, excitement or stupor occurs during a period of nitrogen excretion, while in C type

the phase of mental upset (excitement or stupor) takes place during a period of nitrogen retention. No intermediate B type has yet been discovered.

Gjessing has marshalled evidence to show that the nitrogen phasic change is of primary importance as a determining factor in the periodic mental disturbance of the synchronous-syntonic cases. The pertinent facts are:

(1) The conditions under which his metabolic investigations have been conducted are such as to exclude the possibility of environmental and exogenous factors.

(2) The strictness of his nursing organization and metabolic regimen with the selection of simple, well-tried, standardized chemical tests reduces working error to a minimum and allows the presentation of unequivocal results.

(3) The disturbance of nitrogen metabolism is not secondary to the nutritive or muscular state occurring in the abnormal mental phase because: (*a*) In the A type case the sudden onset of the abnormal mental state occurs *after* nitrogen excretion has already started and not vice versa; and (*b*) in the C type case the abnormal mental state is associated with nitrogen retention despite the increased general metabolism at that time, with a slight fall in body-weight.

(4) Faulty absorption from the gut can be excluded since the fæcal nitrogen remains relatively constant throughout the period of investigation.

(5) The giving of a constant diet induces a regularity in the attacks of stupor or excitement.

(6) When the protein intake is diminished the quiescent interval between two episodes of abnormal mental state is prolonged; when increased the interval period is shortened.

(7) When the body's nitrogen store is depleted by using thyroxin the phasic nitrogen swings flatten out and the mental state remains free from its periodic upset.

(8) A low protein diet after depletion of the body's nitrogen store prevents reaccumulation of nitrogen to the body and this prevention is attended by a freedom from mental symptoms.

These points taken together strongly support the conclusion that the mental disorder follows directly upon a disturbance of nitrogen metabolism, and on them Gjessing has constructed a working hypothesis. He suggests that at the time of change of phase in a varying nitrogen balance a toxic substance, connected with disturbances of protein metabolism is produced which acts in an inhibitive or irritant way on the central nervous system. At the higher levels this toxic substance produces stupor or excitement and at the lower levels produces effects in the autonomic system more or less equivalent to a sympatheticotonia. The patients are unable to deal with a large depot of protein and are functionally normal only when the body's protein store is at a low level.

The extreme care with which Gjessing has conducted his investigations, the presentation of facts about which there can be no doubt taking into account the conditions in which they were obtained, and the stimulating nature of the working hypothesis offered, stamped this work as of tremendous importance in the pathology of schizophrenia (Stokes, 1939). It was our intention to put some of the points to further test.

CLINICAL MATERIAL

Case I.—W. H., male, born 1901.

Family history.—The paternal grandfather died at the age of 75 in a mental hospital where he had been admitted eleven months previously. There is no other history of mental disorder in the family.

Personal history.—The patient's early life was normal although his schooling was considerably interrupted by reason of the family moving frequently from town to town. He worked as a theatre stage hand and had a long period of unemployment between the ages of 20 and 23. His interests were normal and his physical health satisfactory.

His personality was described as affectionate, cheerful and sociable. He was keen on sport and almost fastidious about his personal appearance. Later he became less open, more sensitive, and rather moody. He was ambitious and over-sensitive of his humble home. He was over-interested in the successful outcome of a doubtful claim which the family had on a large fortune in a lawsuit.

Present illness.—At the beginning of November 1924 the patient was excitedly anticipating the outcome of the lawsuit and was keenly disappointed when it was postponed. He looked ill and strange and suddenly pleaded with his parents to get a new home. He wandered about and became very agitated and excited finally abusing his

mother and accusing her of taking money from him. He became unmanageable, spoke of voices calling to him and had to be removed to an observation ward whence he was admitted to West Park Hospital on November 5 under certificate.

On admission.—There were no physical signs of organic systemic disease. He took little interest in his surroundings and lay in bed with his head covered by bedclothes. He resented interference, was suspicious, abusive and truculent. He claimed he was entitled to the S..... millions and argued irrationally. He said his thoughts were being read and that he was subject to some mysterious power. He heard voices which told him he was insane.

Progress.—He remained apathetic and indifferent to his surroundings but believed he was the second Jesus Christ and that various Germans were in the ward working through his head. In 1926 it was definitely noted that pronounced fluctuations occurred in the mental state. In one phase the patient was relatively well, worked hard in his ward and was able to enjoy privileges including going out of hospital. In the other phase he was acutely ill: he was excited, restless, irrational and hallucinated. He gradually became worse, the worsening being apparent in both phases. The phase of grossly abnormal mental state changed to one of stupor; the relative normal phase was marked by vagueness, apathy and a tendency to be more solitary. Since September 1929 the patient has been subject to frequent, recurring attacks of stupor.

The patient has remained healthy from the point of view of systemic disease and his weight has remained constant between 8 and 8½ st. Oral sepsis was eradicated in November 1938. In March 1938 he had received a course of 8 cardiazol injections without effect on the mental state or its phasic change. At the last of these convulsions the neck of the right femur was fractured.

In June 1938 the patient was given sodium amytal intravenously while in stupor. There was an immediate return to the lucid phase but the effects were transient.

On January 1, 1939, the patient was placed under special observation. Apart from the times of stupor he was quiet and docile but with general poverty of movement and lack of initiative. He kept himself clean and tidy and was capable of routine work of a sedentary automatic kind. In marked contrast to this condition his stupor periods came on suddenly, progressed to their greatest depth and then remitted. At such times he would be completely immobile, mute, making no effort to attend to the necessities of toilet. He had to be fed, would make no reaction to commands and was indifferent to stimulation by tickling or slapping. *Flexibilitas cerea* was sometimes prominent. These periodic stupors have persisted up to the present time.

Diagnosis.—Schizophrenia—periodic catatonia—stupors.

Case II.—W. V., male, born 1898.

Family history.—No other member of the family is known to have had mental disorder.

Personal history.—The patient's early life was normal although he was below standard at school and in the labour market was capable only of a number of blind alley jobs. He joined the Army at 18 but was discharged within six months on account of poor sight. He succeeded in rejoining the Colours in January 1918 at the age of 20 and was later sent to the Rhineland with the Labour Corps. He had had no serious illnesses and was abstemious in habits until joining the Army, but then he "drank like a fish", and was very excitable in his drink. His personality was described as sociable and generous. A good mixer, he was popular in company, and preferred company to reading or solitary hobbies. He was not moody but easily worked up.

Present illness.—The onset probably occurred in 1919 whilst the patient was in the Rhineland. He states he was drugged with two other soldiers while entertaining three German girls. When he recovered he found himself in hospital in England. He was transferred to Warrington Hospital and was there five months. No details of this illness are known.

On discharge he was seen to be an entirely changed man. He drank and loafed about with unemployed ex-soldiers. He was "nervy", easily annoyed, morose and had a general "grouch". He only did odd labouring jobs. After a year his grandmother died and this is said to have been a great shock to him. He became childish, "lost his memory" and wandered away from home. His strange behaviour terrified the relations and he was admitted to an observation ward. There he made a homicidal attack on another patient with a table knife. He thought this patient was an evil influence, an agent of the Sinn Feiners, and had tried to poison him with gas. He was admitted to Banstead Hospital on January 27, 1921.

On admission.—His physical health was satisfactory although internal strabismus and myopia were present. An arrhythmia of the heart was present and his pupils reacted

sluggishly to light. His mental condition showed normal orientation, simple and childish conduct, and a continued belief in the ward activities of the Sinn Feiners.

Progress.—At first the patient was relatively well-behaved, although simple and dependant. Seven months after admission he relapsed into a restless and confused state which rapidly cleared up only to return some nine months later. In 1922 it was thought that he had exophthalmos and that his thyroid gland was more prominent. Following tonsillitis in 1923 the thyroid became much enlarged; he had marked exophthalmos, fine tremors of the fingers and tachycardia. In 1924 after further tonsillar sepsis he became restless, resistive and hallucinated. He was given a bad prognosis but physical and mental improvement occurred over a period of weeks.

On November 27, 1924, the patient was transferred to West Park Hospital and since that date until the present he has been subject to attacks of acute excitement. In the "good" phase the patient was generally well conducted, a good worker and on merited parole; at these times hallucinations and delusional ideas were absent or not overt. In the "bad" phase the patient was inaccessible, excited, very restless and acutely hallucinated. The length of the attacks and of the quiescent intervals were usually several weeks and often many months.

In December 1925 the patient developed pulmonary tuberculosis which improved and relapsed in the following winter. In January 1927 he developed gangrene of the right lower limb and in April amputation above the knee was performed. Since that time the physical state of the patient has improved over the course of years. When placed under special observation on January 1, 1939, there was no evidence of thyrotoxicosis, pulmonary tuberculosis, or disease of the peripheral vessels. He was in an excited phase of mental upset. He was not co-operative and lacked in grasp. He was extremely restless with many gestures, and mannerisms. His talk was rambling and usually incoherent. Neologisms were occasionally made out. He was continually distracted by hallucinosis, frequently adopting listening attitudes. He was impulsive and difficult to control. When his attention could be held he was correctly orientated.

Diagnosis.—Schizophrenia in a person of dull intelligence—recurrent excitement.

These two cases were chosen because they seemed from their history to be representative of periodic catatonia and because their swings into abnormality seemed sufficiently frequent to allow a fair return from intensive investigation. Furthermore, the stupor of the one contrasted with the excitement of the other. However, it was soon apparent that the second case, W. V., did not conform to the group of periodic catatonia. His excitement was not clean cut, but varied considerably throughout a day in intensity and quality. Furthermore, it was not attended consistently by a raised temperature and pulse-rate. None the less the investigation on this case was continued in order that he might serve the purpose of a control.

CONDITIONS OBSERVED

(1) The patients were examined for focal sepsis and eradication was carried out by the appropriate treatment. Only dental and oral treatment was required.

(2) All drugs were prohibited and smoking reduced to three cigarettes a day.

(3) A uniform fluid diet accurately made up was given in precise quantities. Tube feeding was employed when necessary. The diet differed in the experimental periods to be discussed, but the same calory allowance was given to the patients throughout. The diet was sampled and Kjeldahl nitrogen estimations carried out daily in the samples. Where dried milks were used arrangements were made to obtain bulk supplies of exactly the same manufacture. This reduced the number of required estimations.

(4) Accessory vitamin factors were added in the form of Nestrovite tablets, one to each patient daily.

(5) The nursing staff were specially instructed and trained to ensure the collection of all urine and fæces and co-operation in technique. The fæces were marked by regular weekly charcoal biscuits. Glycerine suppositories were used twice a week when necessary.

(6) Kjeldahl nitrogen estimations were carried out on all twenty-four-hour specimens of urine and on all stools. They were carried out in duplicate.

(7) The temperature and pulse were taken before meals with the patient rested. The temperature was taken *per rectum*, two separate readings on each occasion. The pulse was taken for a full minute, two separate readings each time.

(8) The stripped weight of the patients was taken twice a week.

(9) The mental state was charted each day in accordance with a simple plan giving a single figure for the degree of motility and lucidity.

Thus: *Motility*:

0- Normal spontaneous activity. Reacting to command positively or negatively.

-1- General spontaneous activity slightly retarded, e.g. tends to stand about. Particular spontaneous activity slightly reduced, stimulated by a joke or insult.

-2- Obviously retarded in spontaneous activity. Speech hesitant and slow. Still stimulated to do things by urging and bullying.

-3- Only occasional spontaneous activity, e.g. shifting his position in bed. Speech limited to a few hesitant phrases. Requires hand feeding.

-4- Short of complete stupor.
Spontaneous activity limited to following with the eyes. Still reacts slightly to command, e.g. putting his tongue out.

-5- Complete stupor—immobile, mute, had to be fed, had to be completely attended to at toilet, no reaction to command, indifferent to stimulation such as tickling, slapping, &c.

Lucidity:

-o- Clearly in touch with surroundings; attention and concentration normal for patient. Insight into illness.

-1- A little vague—thought disorder and hallucinations not overt.

-2- Vagueness more marked—thought disorder and hallucinations obvious without probing.

-3- Vagueness so marked that psychiatric examination difficult.

-4- Complete stupor—no contact possible with thinking processes.

The conditions observed therefore conform to those laid down by Gjessing and indicate the limitations of the method: considerable organization is required, minute attention to detail on the part of the nursing staff is absolutely essential, and the returns are far from speedy.

NITROGEN METABOLISM

Constitution of nitrogen balance curve.—The nitrogen balance curve is made up daily from the estimated nitrogen in the food, the urine, and the fæces, with a correction. The correction is necessary because:

(*a*) Loss of nitrogen to the body occurs in the sweat, in the hair and other skin structures, and in the semen (nocturnal emissions or occasional masturbation). Correction for this must be added to the negative side of the balance.

(*b*) The measured quantity of food is not wholly given since drainage from measuring utensils and drinking cups is not complete. Correction for this must be added to the negative side of the balance.

(*c*) The measured quantities of urine and fæces are less than the actual quantities passed by reason of incomplete drainage. Correction for this must be added to the negative side of the balance.

(*d*) The Nestrovite tablets contain a small quantity of nitrogen which is put into the body. Correction for this must be on the positive side of the balance.

The correction can be counted as a constant daily quantity and without it the nitrogen balance curve steps up. The amount of correction given is just sufficient to stop the stepping up and in our cases this amounted to 0·40 g. a day. Since the greatest loss is due to sweat, this figure is not unreasonable (Peters and Van Slyke, 1931).

The excreted urinary nitrogen over the twenty-four hours can probably be immediately related to the metabolism of the food taken over the twenty-four hours; not so the fæcal nitrogen. The procedure here adopted is to add the nitrogen obtained from all fæcal specimens starting with a charcoal marked one, up to but not including the next charcoal-marked specimen, and to divide that addition evenly over the week, which started with the giving by mouth of a charcoal biscuit. Where the timing of the changes in nitrogen metabolism arises this procedure would make the timing suspect if it were not that the fæcal nitrogen is always a comparatively small quantity. Even so it must give rise to a slight distortion of the real curve.

A typical week's results are as follows (the figures represent grams nitrogen):

Date	Intake food	Output			Output total	Daily account	Running account
		Urine	Fæces	Correction			+3·11
April 18	9·58	12·55	0·54	0·40	13·49	−3·91	−0·80
,, 19	9·84	7·21	0·54	0·40	8·15	+1·69	+0·89
,, 20	9·58	10·82	0·54	0·40	11·76	−2·18	−1·29
,, 21	9·32	10·65	0·54	0·40	11·59	−2·27	−3·56
,, 22	9·84	8·57	0·54	0·40	9·51	+0·33	−3·23
,, 23	9·97	10·21	0·54	0·40	11·15	−1·18	−4·41
,, 24	10·61	9·29	0·54	0·40	10·23	+0·38	−4·03

The running account is the nitrogen balance and this reflects the fluctuation of the bodies' total nitrogen store. The size of that store is not known, but only the degree of change in it.

Experimental Period I. January 11, 1939, *to May* 20, 1939

Case I: W. H., aged 37. Weight 7 st. 12¾ lb. Height 64⅜ in. Basal caloric requirement 1,430 calories.

Case II: W. V., aged 40. Weight 7 st. 3¾ lb. Height 43¾ in. Basal caloric requirement 1,350 calories.

Diet: 480 g. of cane sugar are dissolved with 6 g. of sodium chloride in 605 c.c. water; 500 c.c. of the sugar-salt solution were taken. 6 eggs are well whipped and filtered through muslin, 300 c.c. of the filtrate were taken and added to the sugar-salt solution. To the egg-sugar-salt mixture were added 2,150 c.c. of fresh milk and 750 c.c. of cream. The cream here is the top half of an eight hours standing milk. The whole solution was well mixed and made up to 3,700 c.c. The caloric value is approximately 1 calory for 1 c.c.

Case I: W. H. received 1,850 c.c. over the day in three meals with one tablet of Nestrovite.

Case II: W. V. received 1,750 c.c. over the day in three meals with one tablet of Nestrovite.

Both patients therefore received a well-balanced diet, with adequate quantity of vitamins; the calories supplied were about 30% above basal requirements. Although not confined wholly to bed excepting when ill the patients' activities were restricted to short walks and very light ward duties.

The nitrogen balance curves are shown as starting on January 11, 1939; the diet was started on January 1, 1939.

Case I (*see* fig. 1).—Over the experimental period there is a very definite regular phasic swing in the nitrogen balance curve. The amplitude of the excursion represents a turnover of 15 to 20 g. of nitrogen and the time between the peaks is almost constant at forty days. The body-weight rises steadily throughout the period and the phases of negative nitrogen balance are not associated with any appreciable loss of body-weight. There is a general increase of body metabolism during the time of nitrogen excretion with a rise in rectal temperature and pulse-rate almost wholly co-existent with the negative balance. At a time (shown in cross hatching) when the temperature and pulse-rate were raised by reason of infection (a boil on the buttock) and the bodily metabolism was increased, there is a gain of nitrogen to the body.

The stupor periods, on the whole, are related to the phase of negative balance. The first and third stupors, however, finish at a time of positive balance, and the third stupor begins at a time of positive balance.

Case II.—*Control* (*see* fig. 2): Over the experimental period there is a consistently maintained negative balance with a steady fall in body-weight. The rate of fall of negative balance is almost unaltered when the patient comes out of an illness in which he was very excited. The rectal temperature remains at a relatively constant low figure, and although the pulse-rate is uneven in relation to episodes of excitement it tends to remain at a low level.

Discussion.—The negative nitrogen balance in Case I is not due to failure of absorption in the periods of stupor since the fæcal nitrogen remains almost constant and the urinary nitrogen excretion follows the nitrogen balance curve inversely. Nor is the negative phase due to the evident increase of general metabolism at that time, since during the period of

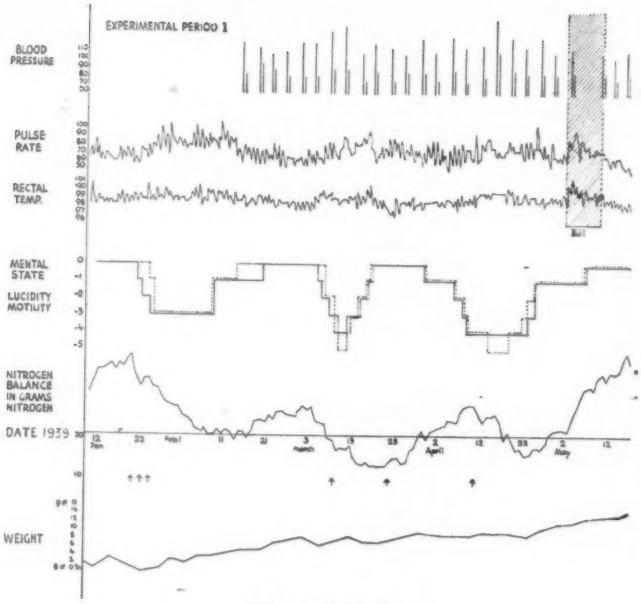

FIG. 1 (*Case I*).

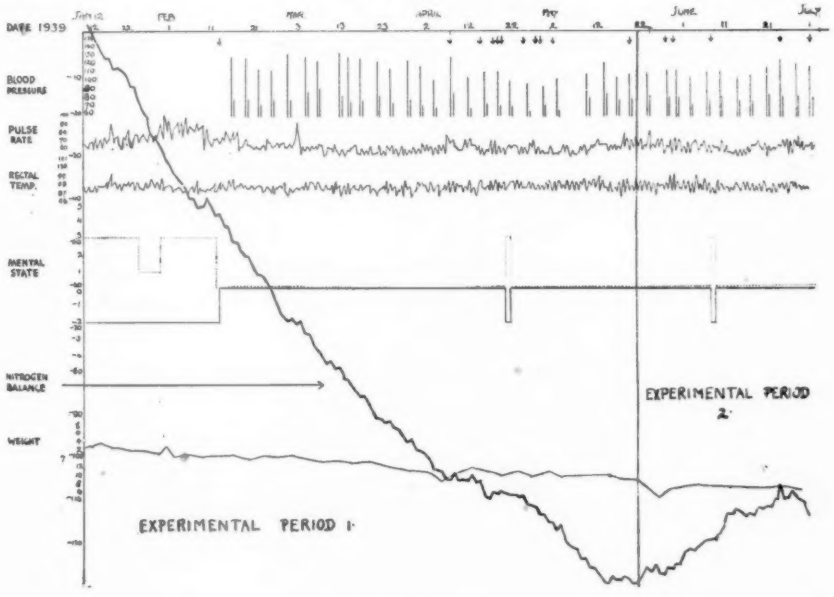

FIG. 2 (*Case II*).

infection there is nitrogen retention. Nor is the nitrogen excretion a secondary consequence of the abnormal mental state, since retention is taking place at some points where the mental state is abnormal. Pertinent to this consideration is the fact that the control case is not over-excreting at a greater rate when acutely excited, although his state of nutrition was deliberately allowed to become poor. The experimental period therefore confirms Gjessing's point that the nitrogen balance swings represent a primary phenomenon under the conditions of experiment.

Experimental Period II. May 20, 1939, *to September* 27, 1939

Diet as in Experimental Period I.

Antuitrin G was given to Case I by injection—26 c.c. were given over twenty days, as shown in fig. 3, the injections coinciding with a period of nitrogen excretion. Following the antuitrin G a considerable protein anabolic effect was obtained over one hundred days. The general upward trend of the nitrogen balance curve is, however, interrupted by periods of negative balance so that three definite peaks in the curve are apparent. These peaks maintain the time sequence of those of Experimental Period I. The increase of rectal temperature and pulse-rate again is seen at the time of nitrogen over-excretion, but the

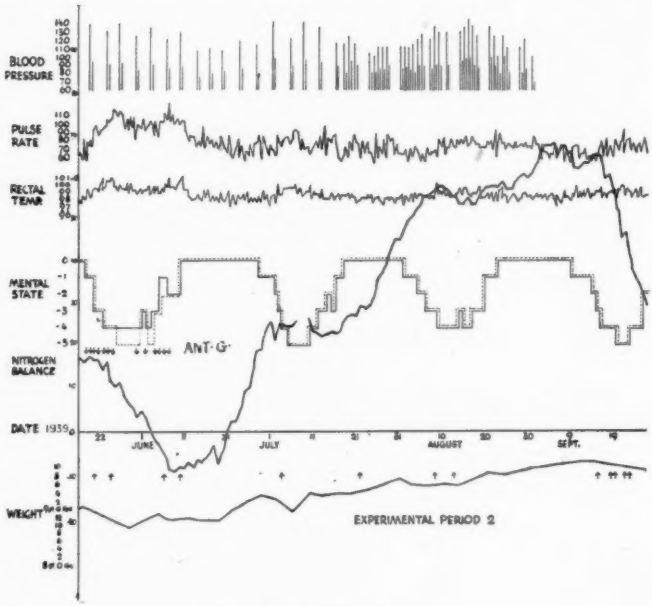

FIG. 3 (*Case I*).

timing is not so consistent. The effect on temperature and pulse is most marked at the period of antuitrin G administration. Again the stupor periods coincide with phases of negative balance, but in the third stupor particularly nitrogen retention occurs at the beginning of the stupor phase. Over the whole experimental period there is a gain of some 50 g. nitrogen and the body-weight steadily increases.

The control case (figs. 2 and 4), to whom no antuitrin G was given, shows in general a positive balance over the period and 50 g. of nitrogen are gained to the body with the maintenance of constant body-weight. The nitrogen balance curve shows a phasic tendency with two peaks during the period. There is no associated mental disturbance with either retention or excretion other than small items of irritable conduct lasting

for a few minutes or hours. The rectal temperature and pulse do not vary with the changing phase of nitrogen metabolism.

Discussion.—Antuitrin G was given to Case I in this experimental period to produce a protein anabolic effect. The intention was to reverse the process accomplished by Gjessing in his use of thyroxin, to bring about a retention of nitrogen and possibly prolonging the stupors or increasing their frequency by this means. That antuitrin G has a protein anabolic effect in animals has been shown by Gaebler (1933) and Shaffer and Lee (1934). It was thought that the preparation and dosage used would produce this effect in man. A general protein anabolism was obtained, but that this was due to the antuitrin G was made improbable by the time lag and by the fact that the control showed a similar quantitative effect over the same period.

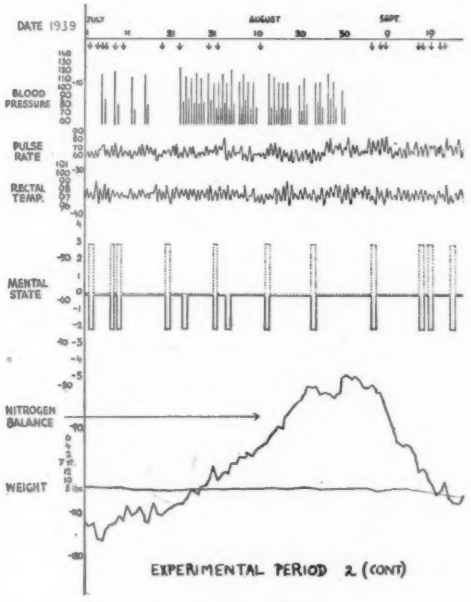

FIG. 4 (*Case II*).

The explanation of the general uptrend of the nitrogen balance curves in both instances is better explained by the increasing richness in protein of the summer milk used in making up the diets. Thus the amount of protein put into the patient W. H. at different times of the year when the volume of diet is kept constant is shown in the following table:

Ten days' period		Quantity of nitrogen
January	11—20	88·14 g.
February	15—24	95·02 ,,
March	12—21	93·09 ,,
April	12—21	97·62 ,,
May	1—10	100·47 ,,
June	11—20	105·00 ,,
July	11—20	110·33 ,,
August	13—22	117·83 ,,
September	6—15	94·66 ,,

These figures explain the general uptrend of the curves between May and the end of August and the down trend in September. They do not explain the periods of negative

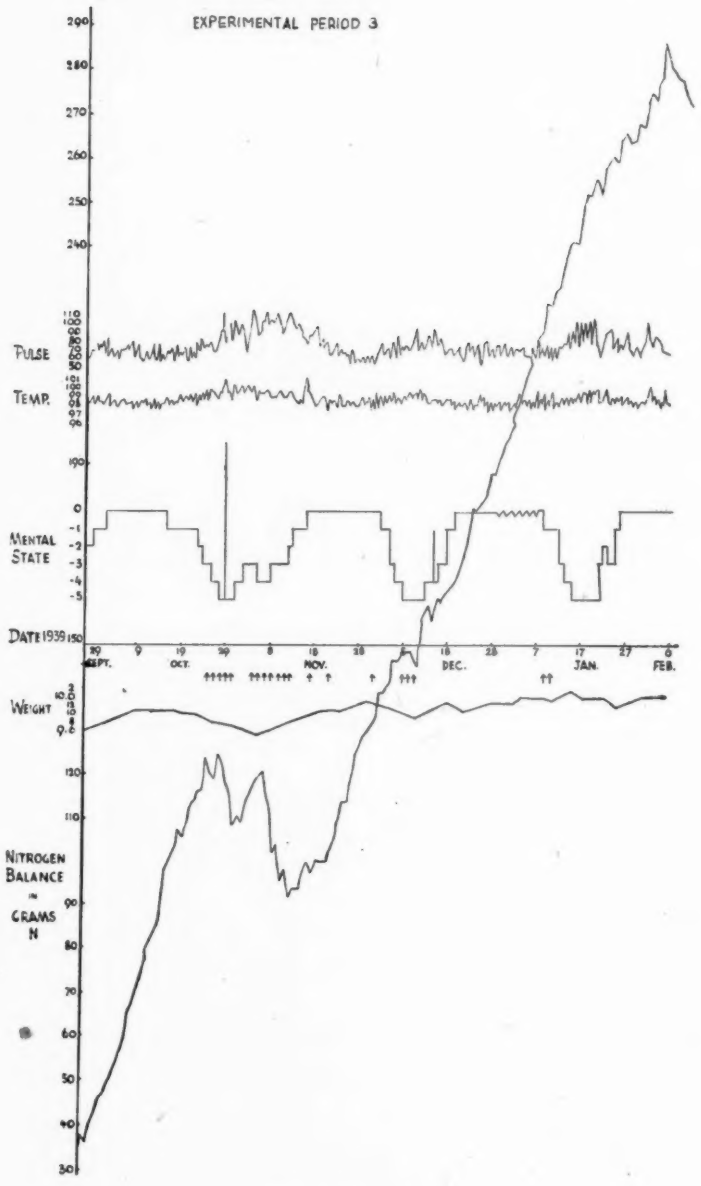
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FIG. 5 (*Case I*).

balance over that time. Similarly the factor of increasing richness of milk does not explain the negative balance period in the control case.

The negative balance in the control patient is not explicable by an infective process operating at that time or an alteration of work regimen. The conditions of experiment were the same as those that had previously operated and an endogenous metabolic factor must be at work. The change is not so clear-cut or so rhythmic as that which occurs in Case I, but it exists unattended by an abnormal episode of mental disturbance or by variations in rectal temperature and pulse.

Whatever the effect of antuitrin G the variation in milk richness allows the testing of Gjessing's hypothesis that by increasing the amount of protein in the diet the quiescent interval can be shortened and vice versa in cases of periodic catatonia. In Case I in the period January 23 to April 25 there are 47 stupor days out of a total of 92; in the period May 21 to August 20 (when the protein intake was greater) there are 50 stupor days out of a total of 91. Only days of stupor deeper in degree than -1 are considered, since the 0 to -1 grade is the most indefinite, and this obviously would weight the first period unduly if counted.

The ratios 47:92 and 50:91 are too near to support Gjessing's thesis. In this patient it can be said that increasing the protein in the diet does not diminish the quiescent interval.

Experimental Period III. September 27, 1939, to February 7, 1940

Diet.—Case I: W. H. Prolac—400 g. a day.
Calory value 1,900.

Percentage composition:	Fat	19·5.
	Protein ...	40·0.
	Lactose ...	29·5.
Protein composition:	Casein	130.
	Lactalbumen ...	10.
	Lactoglobulin ...	1.

Case II: W. V. ½ cream Cow and Gate—400 g. a day.
Calory value 1,800.

Percentage composition:	Fat	15·0.
	Protein ...	20·0.
	Lactose ...	58·0.
Protein composition:	Casein	60.
	Lactalbumen ...	10.
	Lactoglobulin ...	1.

Over this experimental period Case I (fig. 5) shows in general a marked positive balance taking up 250 g. of nitrogen in the time covered. The ascent in the curve begins immediately. There is one definite period of negative balance coinciding with the first stupor. A feature to be taken into account is the vomiting that occurred in this stupor (indicated by the arrows). The vomiting occurred at the time of feeding and the vomit was always collected, measured, and could usually be regarded as neat food and allowed for. None the less the curve is unsatisfactory by reason of it, although the negative balance is certain. More doubtful is the small negative balance coinciding with the second stupor. The third stupor is not associated with a negative balance. The rise of rectal temperature and pulse-rate occurs at the time of stupors as before, but here it is divorced from an over-excretory phase of nitrogen in the third stupor, and to all intents and purposes in the second stupor. The body-weight shows a steady rise throughout. The stupors continue to develop at the same time-interval.

The control case (figs. 6 and 7) shows a continuation of the downward trend of the nitrogen balance curve although the protein intake is greater than in the previous experimental period. This trend continues for eighteen days, when a reversal to positive balance occurs. At a time of retention, acute excitement suddenly breaks out, and associated with the excitement there is a plateau effect followed by an irregular downward tendency in the nitrogen balance curve. The body-weight remains constant throughout. The pulse is raised in relation to the excitement, but not consistently so, and the rectal temperature remains at a relatively constant level.

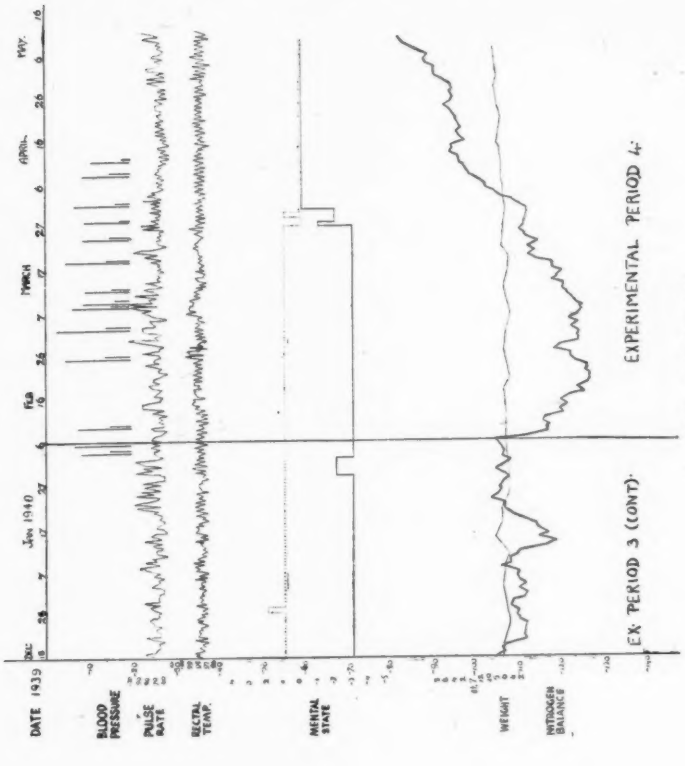

FIG. 7 (*Case II*).

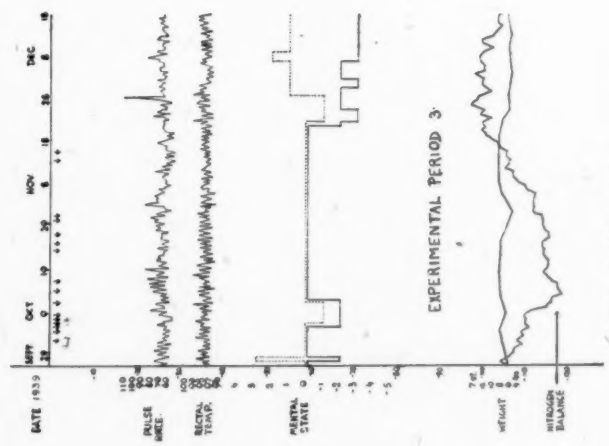

FIG. 6 (*Case II*).

Discussion.—In this experimental period dried milks were used in order to lessen the number of analyses. On the whole they were more constant in protein content than fresh milk, but were not, at first, tolerated so well.

The protein intake in Case I was doubled and it is obvious that the patient can readily store protein. Furthermore, when the storage is proceeding at a quick rate the stupors continue in regular sequence. It is evident that stupors can occur without nitrogen over-excretion. In this connexion it might be thought that if a partition of the total protein was being over-excreted it would be "buried" in the curve. However, the curve rises in almost a straight line over the time covered by the last two stupors and no excretion quantitatively equivalent to that occurring in Experimental Period I shows itself.

At the lowest level of stored nitrogen in the Experimental Period under investigation, a stupor is associated with a negative nitrogen balance, but, when the ascending nitrogen balance curve reaches 150 g., for the first time there is no over-excretion (or almost none) associated with stupor. Nor does this association ever recur in our experiments—a point to be taken up in Experimental Period IV.

Since it is apparent that the increased rectal temperature and pulse-rate are linked with the stupors and not with nitrogen negative balance the significance of these phenomena must be sought in connexion with the stupors and not in connexion with protein metabolism.

The control case offers a marked contrast to the true periodic catatonic patient in two particular respects: first the plateau effect in the nitrogen balance curve, and secondly the absence of consistently raised temperature and pulse *despite* excitement.

It is to be noted that the findings in Case I conflict with Gjessing's working hypothesis. The high protein diet has not altered the stupor sequence and stupors occur without phasic change of nitrogen balance.

Experimental Period IV. February 7, 1940, to June 15, 1940

Diet.—Case I: W. H. ½ cream Cow and Gate—400 g. a day.
Calory value 1,800.

Case II: W. V. ½ cream Cow and Gate—400 g. a day.
Calory value—1,800.

Over this experimental period Case I (fig. 8) shows an initial drop in the nitrogen balance curve, independent of stupor, followed subsequently by a consistent ascent without negative balance at the times of stupor. The body-weight is constant over the period. The pulse and temperature continue to rise significantly at the time of abnormal mental state.

The control case (fig. 7) was carried only until May 11. Over the period of excitement the nitrogen balance curve drops and then rises. For at least four weeks the patient has a positive nitrogen balance despite his excitement, and on return to normal mental state the rise in balance is maintained. Over the period the body-weight remains constant. The rectal temperature does not alter its base line, although the pulse becomes less irregular when the patient's excitement subsides.

Discussion.—The experimental conditions for Case I over this period of investigation differ from those obtaining in Experimental Period I thus: (*a*) The calory value of the diet is a little lower; (*b*) no egg proteins are in the diet; (*c*) the ratio of protein : fat : sugar in the diet has been altered; (*d*) the body-weight is at a higher level by approximately 2 st.

Under these new conditions no swings in nitrogen balance occur, whereas in Experimental Period I they were very evident in relation to the stupor phases. The slight difference in calory value is not a sufficient explanation. Furthermore, no egg protein was used in the diet in Experimental Period III, although there was one phase of negative balance then. Explanation of the discrepancy might well be found in the differing composition ratios of the diets and further work is required to investigate this factor. However, the simplest explanation is in the differing state of nutrition of the subject in the two periods as shown by body-weight. Up to November 18, 1940 (Experimental Period III) the patient's nutritional state has been such that he has had to draw on his protein store to support the increased metabolism of the stupor period. After that time his nutritional condition allows the sparing of his proteins. This simplest explanation conflicts with that offered in Experimental Period I, where parts of some of the stupors

were associated with a period of nitrogen retention, and where the increased metabolism of infection did not bring about a negative balance. Furthermore, it is against the evidence offered by Gjessing in connexion with his C type cases where in the active phase of mental disorder there is nitrogen retention. Härn also has obtained period swings in the nitrogen balance curve associated with the active phase of mental disorder in a periodic catatonic on a high calory diet. Further work is therefore required to co-ordinate these apparent discrepancies. The present work had to be stopped in its intensive aspect at this point owing to the war.

The control case indicates that nitrogen retention can occur despite intense excitement and motor activity, when the nutritional state is poor.

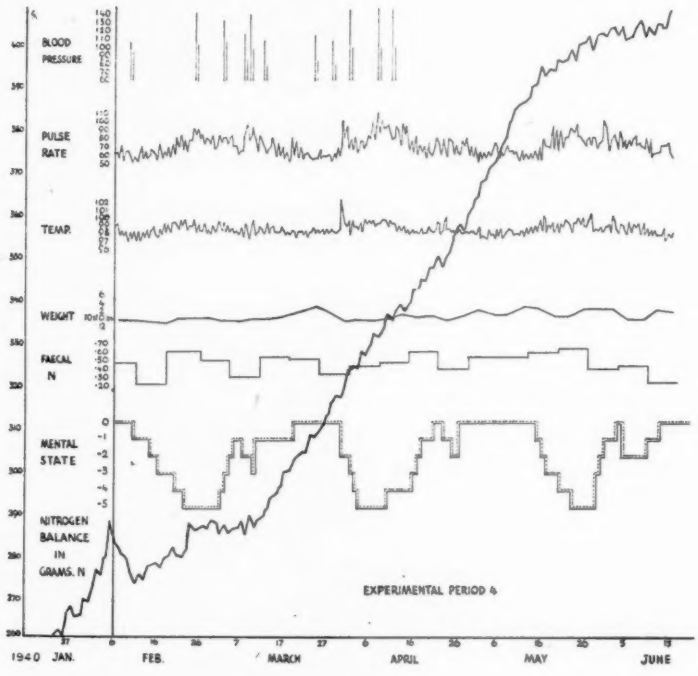

FIG. 8 (*Case I*).

Experimental Period V. June 15, 1940, to *May* 11, 1941

Diet.—Case I: W. H. Ordinary ward diet.

Following the intensive investigations on constant diet the patient was allowed to return to ordinary ward routine conditions. His stupors recurred in uninterrupted sequence, although his weight dropped from 10 st. 2 lb. to 8 st. 5¾ lb.

CONCLUSIONS

In one case of periodic catatonia it is concluded that: (1) significant modifications in mental state are not produced by intervention in protein feeding; that increasing or diminishing the protein in the diet does not disturb the rhythm of mental disorder, nor does relatively irregular feeding of protein; (2) from nitrogen balance estimations a phasic association of stupor with a negative nitrogen balance occurs until a high level

of general nutrition (as indicated by a rising body-weight) is attained; above this critical level there is mental disorder without nitrogen over-excretion; (3) there is a weight of evidence against the simplest view that the nitrogen change is secondary to a mental disturbance which requires the breaking down of protein for the production of calories; (4) whatever the explanation of the phasic association may be the protein metabolic change is not *immediately* causative to the mental upset; (5) in a case not periodic catatonic a rhythmic tendency of nitrogen balance was found without mental upset.

AUTONOMIC DISTURBANCES

Throughout all the periods of investigation the association of increased pulse and rectal temperature with stupor has been invariable in the case of periodic catatonia. This association has not been present in the excitements of the control case. Furthermore, blood-pressure readings in periodic catatonia show a marked rise regularly produced in association with stupor, a phenomenon markedly in contrast with that which occurs in the control case. This conforms to Gjessing's more detailed and ampler observations in his synchronous-syntonic group both A and C type. The association appears to be a fundamental one and requires further elucidation.

Dr. Hardwick

ENDOCRINE DYSFUNCTION AND THYROID THERAPY

For many years the field of endocrinology has been searched for an ætiological factor in schizophrenia. Mott's studies on the atrophy of the testes seems to offer a solution, but his work has been severely criticized (e.g. by Morse and Lewin), and it has not fulfilled its promise. In general, no specific disorder of the endocrine glands has been found; nor is this really surprising, for, as Hoskins points out, if we postulate endocrine abnormality as an important factor we have to account for the fact that it is limited to relatively minor manifestations.

In these widespread investigations into endocrine disorder, the clinical features of some cases of schizophrenia pointed to possible hypofunction of the thyroid gland. Thus, a pasty, thick and inelastic skin, a slow pulse, low temperature and clinical evidence of lowered metabolism, together suggested a hypothyroid state. Lowered basal metabolic rates seemed to confirm the clinical impressions. Thyroid preparations were given to correct the assumed hypothyroid factor (e.g. Leeper, Lewis and Davies, Minski). These latter workers were guided by clinical sense in their choice of cases and did not use methods of biochemical control. Favourable results were reported despite the pessimism of Kraepelin, Witte, Lewin and others to this form of treatment. Later Hoskins and Sleeper, and Lingjaerde selected cases of schizophrenia with low basal metabolic rates for thyroid medication. They, like Minski, used large doses, but used them over long periods, noting that as a rule they were well tolerated. More recently, Sargent, Fraser and Brazier have given thyroid to patients in whom the impedance angle values were low (Brazier units). They claimed that such cases were much improved, and they confirmed a high tolerance. Their work had been stimulated by that of Gjessing.

Gjessing has had to consider carefully whether or not the activity of the thyroid gland was specific in producing the phasic disorder characteristic of periodic catatonia. The following points constitute the main evidence available:

First, in the "normal" or inactive phase of his A type of case there is torpidity, a dull inactive skin, low temperature, and a slowish pulse suggesting lowered thyroid function. In the abnormal, or active phase, there is some protrusis bulbi, an increased pulse-rate, a higher temperature level, and tremor, suggesting increased thyroid activity. One must admit that these clinical facts *per se* are impressions only of disturbed thyroid function.

Second, the basal metabolic rate is considerably increased in the abnormal phases (20 to 30%); this applies when the abnormal phase is one of stupor or one of excitement. Such findings are consistent with the clinical impression. However, the raising of the basal metabolic rate cannot be accepted alone as an indication of thyroid function—it may be an expression of general autonomic disturbance, such as might occur with fever or in toxæmia.

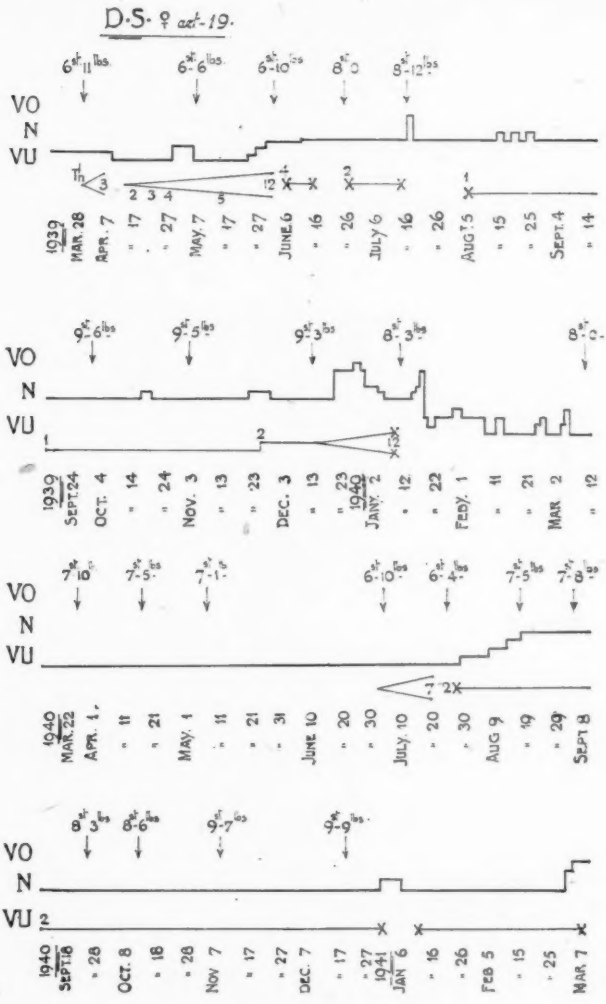
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FIG. 1 (*Case I*).

Third, the electrocardiogram in the normal phase of type A shows a flat T_1 wave resembling that found in myxœdematous patients and in anoxia. The T_1 wave after a temporary exaggeration returns to normal. In the type C case similar electrocardiograph changes occur from phase to phase, but in this group the flat T_1 waves are found in the abnormal phase. Then, if a flat T_1 wave is to be considered evidence of reduced thyroid activity, it is inconsistent with the increased pulse-rate, increased oxygen consumption, &c., found in the reactive phase of the type C case.

Fourth, the impedance angle. Gjessing has found a diminished impedance angle in the active phase of his C type case, and in our work (Brazier, Hardwick and Stokes—to

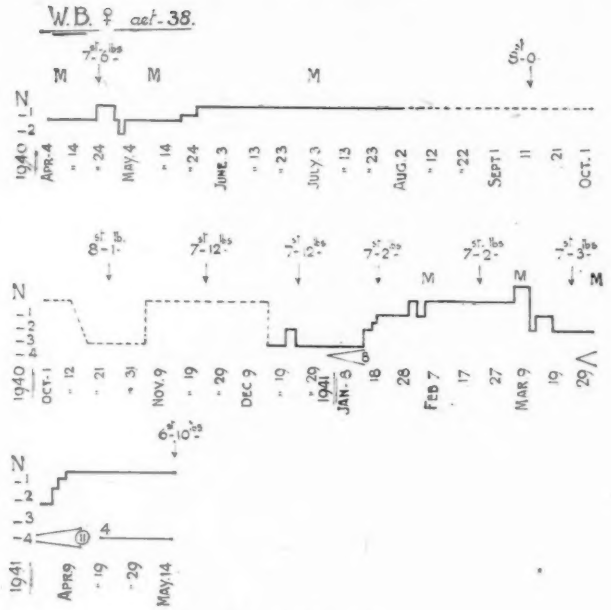

FIG. 2 (*Case II*).

KEY TO ALL CASES (HARDWICK)

(1) The abscissæ represent the dates.

(2) The ordinates represent a graphic indication of the mental state.

V O = Very overactive. (Mental state one of pronounced excitement.)
O = Overactive. (Mental state one of excitement.)
N = Mental state normal, or relatively normal (quiescent phase).
V U = Very underactive. (Mental state one of stupor.)

In Charts 2 and 4 the following figures occur directly beneath " N ".
−1 = Slight reduction in activity.
−2 = Mild Stupor.
−3 = Moderate stupor.
−4 = Deep stupor.

The continuous line of the patient's mental state is replaced by an interrupted line in two instances. This signifies the estimated mental state, since the patient during the period covered by the interrupted line was not accurately observed and examined daily.

(3) The thyroid administration is shown by crescendo markings or horizontal lines immediately beneath the graph of the mental state. (Th = thyroid.) The figures represent the number of grains given per day. The horizontal lines indicate a fixed, regular daily dose, the amount per day being indicated by a figure. The crescendo markings indicate an increasing dosage of thyroid up to a maximum which is shown by the figure lying between the two arms of the crescendo marking.

(4) M = Menstruation.

(5) The weight markings are self-explanatory.

be published) there is a diminished impedance angle value in the stupor phases of an A type case. These findings are obviously inconsistent with the clinical observations, B.M.R. estimations, and electrocardiograms, if considered only in terms of thyroid function.

It is therefore doubtful if there is a specific thyroid factor operating in periodic catatonia. The positive evidence is not conclusive and there are important anomalies which yet await explanation.

Gjessing joins issue on these points and does not use his thyroid treatment as a substitute for hypothetical hypothyroid function in his cases. He uses it to catabolize body nitrogen in order to compensate for a disordered nitrogen metabolism. This he considers necessary on the assumption of the formation of a toxic substance associated with the phasic storage of nitrogen. He holds that this toxic substance produces an irritant effect on the vegetative centres, and stupor or excitement results. If the storage of nitrogen is prevented, the formation of the toxic substance should be prevented and, he argues, the stupor or excitement should not occur. In the treatment of his cases he has therefore placed them on a low protein diet and has given thyroxin in an ascending scale of dosage up to the point of mild intoxication. With the subsidence of the intoxication he has continued with the diet, and thyroid gland extract is given to maintain the nitrogen depletion.

Cases from the female side at West Park Hospital were selected for treatment with thyroid. Thyroxin was not exhibited, but the same standard brand of thyroid extract was used throughout the experiments. The cases have been followed simply on clinical criteria and have not been the subject of biochemical investigation.

During the periods of thyroid medication the patients, with one exception, have had a relatively low protein diet. All meat was excluded, fish given only twice a week and only one egg allowed each day. Otherwise the ordinary ward diet was permitted, and this was supplemented by soups, vegetable stews and milk dishes. During the active phase of treatment the patients were in bed. The results were as follows:

Case 1.—D. S. This case is that of a young girl of 19, of simple and probably defective parents. The patient herself is defective, with an I.Q. of 68-77. Her first attack of mental disorder occurred at the age of 15, and on the second attack she was admitted to the Maudsley Hospital in a state of stupor. She improved on thyroid but in less than three weeks after its omission she relapsed into an hallucinatory state. Before her admission to West Park Hospital there is a history suggestive of two separate attacks of stupor.

The chart represents a record of the fluctuations in her mental state whilst in hospital. The abscissæ represent the dates and the ordinates a graphic indication of the mental state. "N" represents the quiescent, inactive, relatively normal or normal state; "V.O." =very overactive (i.e. where excitement is the predominant mental feature); "V.U." = very underactive. Note that different gradations of the degree of stupor, or excitement, are represented, the assessment of these values being determined by arbitrary standards and necessarily by daily observation and examination of the patient.

It will be seen that the patient was initially in a state of stupor. On March 30, 1939, thyroid treatment was commenced. From April 12 the dosage was gradually increased in stepladder fashion until May 30, 1939. The administration of thyroid is indicated on the chart as shown, the figures representing the number of grains given per day, and the increasing dosage being represented by the crescendo-like figure. A total of 12 gr. *per diem* was reached before mild toxic symptoms ensued. It will be seen that the mental condition begins to improve actually before the maximum dose is reached. On June 4 the maintenance dose of thyroid is commenced (4 gr. per day), eventually reduced to 1 gr. per day. The gaps indicate temporary cessation of treatment as mild toxic symptoms persisted during these periods. After remaining in a nonactive phase for several months (apart from short periods of mild excitement), the dosage was again increased in stepladder fashion on November 24 for experimental reasons, and discontinued again when a maximum of 12 gr. per day was given. Here it will be noted that the patient passes into an excited state whilst the drug is being increased, and that with its complete cessation, the patient relapses into a stuporose condition. A further experiment on July 1, 1940, indicates a somewhat similar result to that seen when the first stepladder thyroid was given, but here the mental condition improves after the maximum thyroid dose, which in this instance was 7 gr. a day only. Then, with a maintenance dose of 2 gr. a day the patient remains in her normal phase until February 28, 1941, when excitement again sets in.

In this case of recurrent stupor it appears that when thyroid is administered in increasing dosage, a change in mental phase occurs. On two occasions a stupor is replaced by a normal phase, and on one occasion a normal phase is replaced by an overactive one. A relatively small daily dose following the intensive course would seem to "keep up" the level of the mental state, and perhaps if administered over a long period, or if sharply increased, tends to push the level further up towards the overactive.

Note that with improvement in the mental state, the weight increases to reach a relatively high level, despite the continuation of thyroid.

Case II.—W. B., aged 38, is a high-grade defective patient who has had recurrent mental disorder since the age of 15. During her three admissions to West Park Hospital since 1927 she has had recurring attacks of stupor (with some features of depression). In

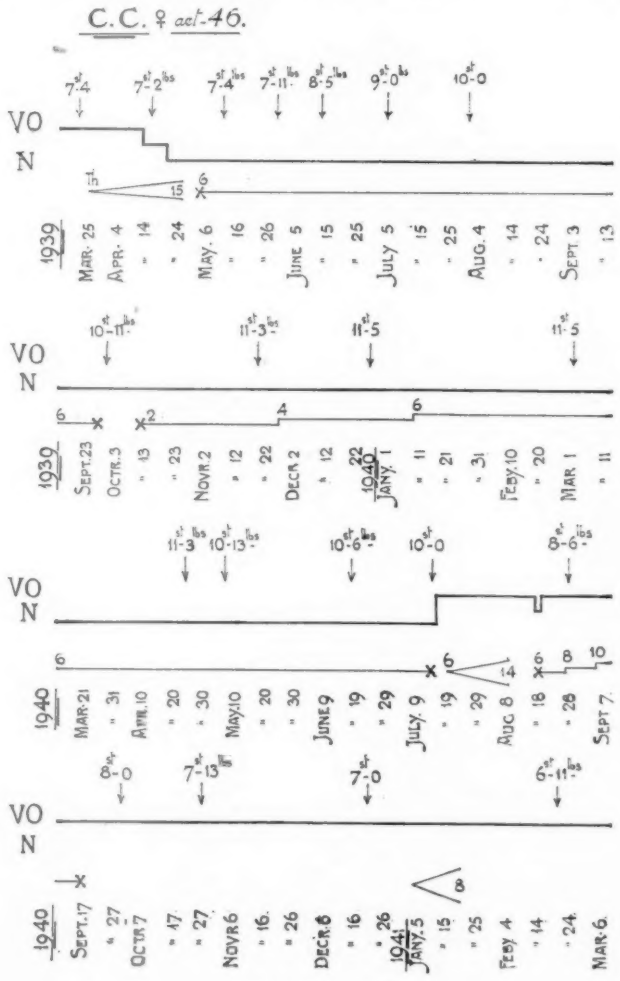

FIG. 3 (*Case III*).

the inactive phase she is a rather dull and apathetic patient but she is not definitely hallucinated.

The chart shows firstly a natural recovery from a stupor phase, a relapse (shown by the dotted line, indicating that the patient was not then under special daily observation). Stepladder thyroid up to a maximum of 8 gr. a day, given at the beginning of the year, whilst in a stupor phase, was followed immediately by improvement and return to "normal". After a partial relapse, a further intensive course is accompanied by a similar return to "normal".

This case of periodic catatonia apparently shows similar responses to thyroid therapy as in the first case, the mental state changing from stupor to normal phase during, or shortly following, increasing dosage of thyroid.

Case III.—C. C., aged 46. This again is a case of recurrent mental disorder—since the age of 19. Her first admission to West Park was in 1924. Her illness has been characterized by long periods of excitement (up to a year, or longer) with relatively short quiescent intervals. In 1932, however, on her first readmission, she was diagnosed as stupor. In January 1939 she was very excited, restless, noisy, overactive, manneristic and destructive; her behaviour suggested hallucinosis. Stepladder thyroid was instituted as shown and before its termination improvement had set in, in the mental state. Maintenance thyroid followed and her mental condition remained relatively normal over a year. On July 12, 1940, thyroid was omitted because of mild toxic symptoms and she relapsed into an excited state two days later, which has persisted since despite an attempt at correction with large thyroid doses.

In this case of periodic catatonic excitement thyroid therapy appears to produce a remission on one occasion, and it appears to fail on the occasion of a relapse. The reason for these findings is not clear, although the temperature and pulse charts for August and September suggest that an increased tolerance to thyroid had developed. Note that, as in Case 1, the weight significantly increases during the prolonged administration of thyroid in the normal phase.

This patient is, at the present time, still in an excited state, and it is proposed to try a further course of thyroid.

Case IV.—A. J., aged 50. This patient is known to have been mentally ill on and off for at least twelve years. During her stay at West Park Hospital between 1928 and 1934, she was known to suffer from recurrent attacks of stupor. Since her readmission in November 1939 the same phenomena have been observed. Examination of the chart shows some lessening of the depth of stupor following the first course of stepladder thyroid, which, however, is short-lived. The second course shows hardly any perceptible change, despite the fact that well-marked toxic symptoms occurred with the relatively small dose of 8 gr. a day.

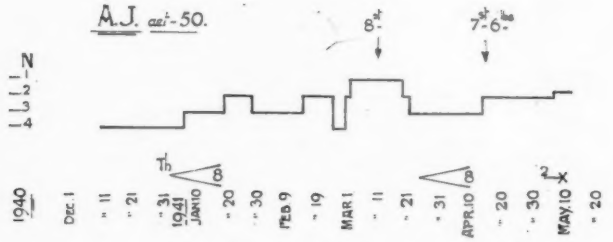

FIG. 4 (*Case IV*).

Thyroid therapy then, in this case, gives doubtful results. Although this schizophrenic patient has recurrent cycles of disorder, there is some doubt if her case fits in with the strict Gjessing S.S. type. Further, the intolerance to thyroid in relatively moderate doses has to be taken into consideration. Note also the sharp drop in weight whilst on thyroid.

Case V.—M. A., aged 49. This interesting case had her first breakdown at the age of 22. Since then, her illness has been characterized by frequent alternating cycles of abnormality and normality. The abnormal phase sets in and ceases abruptly and presents many constantly recurring features. Hypermobility, impulsiveness, grimacing, explosive laughter, mischievousness, pointless pranks, alternating expressions of elation and anger are some common symptoms. Hallucinosis appears often to be present. In the normal phase there is little apparent evidence of mental abnormality.

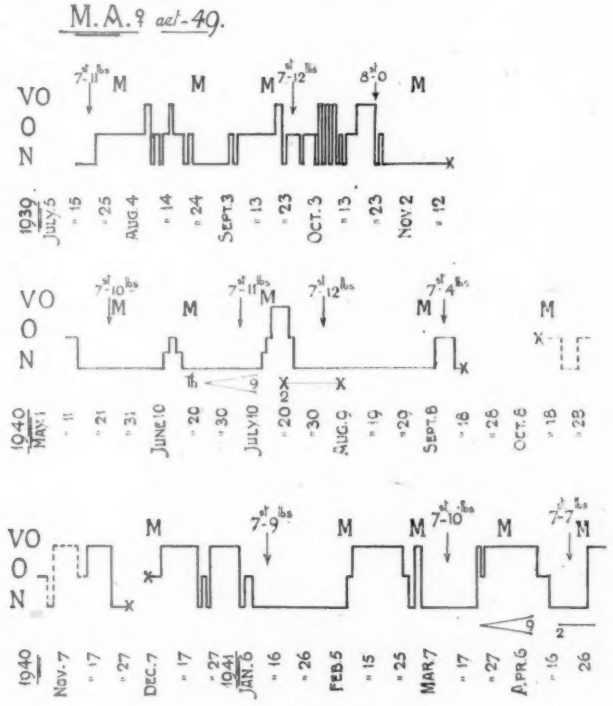

FIG. 5 (*Case V*).

The upper chart demonstrates the irregularity and frequency of her swings. Thyroid was administered as shown on the middle chart during a normal phase, but an overactive phase followed. Thyroid was not maintained for any length of time as the patient tolerated it poorly. A second stepladder course given recently is shown in lower chart, when a normal phase quickly follows. Nevertheless, despite maintenance thyroid, a further swing to abnormality occurs.

In this case it is doubtful if thyroid has any beneficial effect, or influences the swings in any way. However, her clinical condition does not fit in well with Gjessing's group, the cycles being very irregular, and the excited condition suggesting a manic component.

Case VI.—J. W., aged 39, is known to have had recurrent psychotic attacks since the age of 17. Her illnesses have been characterized by strange, bizarre conduct, overactivity, impulsiveness, and irrelevant and irrational conversation. During her periods in mental hospital the abnormal phase has lasted for many months. On the occasion of her admission in September 1938 she remained in her excited condition up to the point indicated on the first graph (March 1939). Stepladder thyroid was given as shown and before the maximum was reached, the mental condition had reverted to normal.

Note the sudden change in this case. She was discharged on August 30 and went back to her work. She continued with maintenance thyroid out of hospital except for the two weeks prior to readmission. She was readmitted on May 6, 1940, at her own request, as she was perturbed by family worries and felt she might relapse. Despite a continuance of maintenance thyroid she relapsed into her active phase, presenting the usual symptoms. A sharp increase in thyroid was followed by a rapid improvement and a return to the normal phase as shown. She has since been discharged from hospital.

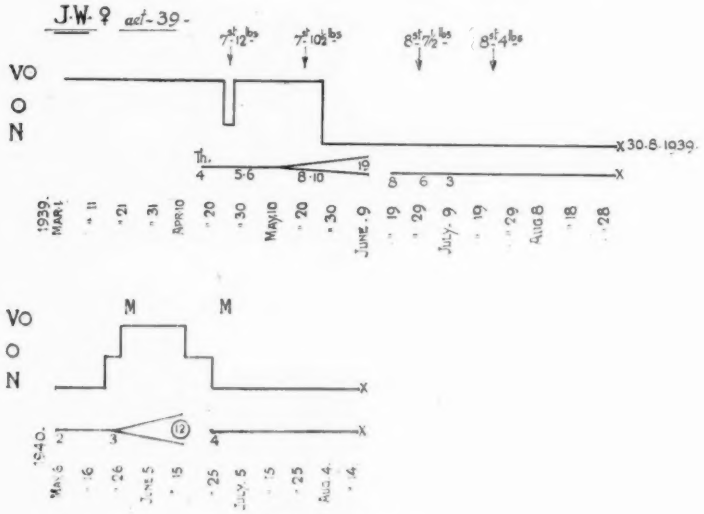

FIG. 6 (*Case VI*).

This case then shows satisfactory responses to thyroid therapy. The relapse was of brief duration and it is possible that it may have been averted if there had been no hiatus in the maintenance thyroid. The patient's weight increases under treatment.

DISCUSSION

The number of cases presented is very small, but it must be emphasized that they represent a highly selected group. For example, at West Park during a period of two years, these cases were selected from approximately 2,000 female patients. Even so, some of the cases chosen raised doubts as to whether they conformed strictly to the group which Gjessing investigated. Thus Case V (M. A.) still has profuse, irregular menstrual cycles at the age of 49, and the features of her case suggest perhaps a fusion of manic-depressive and schizophrenic tendencies. The other cases do conform with Gjessing's criteria with the possible exception of Case IV (A. J.), who might well belong to his A.A. type. And, with the exception of this case, they do appear to respond to thyroid medication, although some degree of failure was encountered. According to Gjessing's working hypothesis, patients who are maintained on a relatively constant low protein diet under thyroid treatment should over-excrete nitrogenous substances and, following this adjustment of their nitrogen metabolism, should become symptom free. That this has not occurred in every instance may be due to inadequate thyroid dosage (patient A. J., aged 50, did not tolerate large doses of thyroid very well), to the faulty timing of the thyroid medication (Gjessing makes a point that the timing of the therapy must be related to the abnormal phase differently in the A type as compared with the C type), or to the fact that the thyroid effect in regard to nitrogen catabolism is not the whole story.

The findings of the nitrogen balance in the patient W. H. seem to point to the last, and it appears that Gjessing's working hypothesis is an oversimplification. However, on the whole, thyroid therapy has a salutary effect on cases of periodic catatonia despite difficulties in explaining the *modus operandi*. Further study is obviously indicated—for example, into the question of dosage, and, for example, into the question of age, since Gjessing himself points out that good results are easier to obtain in young and recent cases than in the older and more chronic ones.

The probable clinical criteria for the exhibition of thyroid are:

(1) A definite rhythmic illness of periodic catatonic type in which

(2) the phases of illness are always associated with sudden definite increase in temperature, pulse-rate and blood-pressure;

(3) the patient tolerates thyroid treatment well; and

(4) there is gain of weight under such treatment.

In reviewing the literature one sees a resemblance in many of the cases successfully treated with thyroid with those of periodic catatonia. Thus some of Minski's cases had passed from a maniacal-like condition into stupor before treatment was instituted—and he used heroic doses. Even Leeper's cases (1900) show some points of resemblance. Mayer's case (1914) was a catatonic subject who, under treatment, went through a manic phase before he became free from gross symptoms. A case of Hoskins and Sleeper reported in some detail improved with thyroid, relapsed into stupor when it was discontinued and responded successfully later.

Conclusion

The work under review points to urgent problems awaiting solution. In relation to the nitrogen metabolism, the effect of varying diets in Gjessing's C type case would appear to be crucial. Investigation of quickly swinging manic-depressive cases, and of women with phasic mental disturbances, is required. Are there endocrine disturbances more fundamental than the periodic nitrogen swings? Richter (1927) has produced cyclical changes of activity in animals by interference with the endocrine elements, and has discussed his results in relation to the manic-depressive psychosis.

Whatever questions remain unanswered, Gjessing, by his painstaking and detailed work in an isolated small field in the vast territory of endogenous schizophrenia, has opened up problems and lines of research, which should bear fruitful and profitable results.

This work could never have been carried out without the active help and co-operation of Professor F. Golla, Professor S. Nevin, Professor E. Mapother, Dr. N. Roberts and Dr. W. A. Caldwell, past and present medical superintendents of West Park Hospital, and especially the nursing staff at West Park Hospital. To these and many other helpers we offer thanks.

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Section of Psychiatry

President—C. P. SYMONDS, M.D.

[*June* 24, 1941]

Amnesic Syndromes in War

By WILLIAM SARGANT and ELIOT SLATER

Loss of memory is much commoner in soldiers in war-time than in civilian practice in peace. From the previous records of some of our patients, it seems that the condition is often overlooked in civil life; in the Army a stricter routine and discipline make this impossible. Attention in the past has been mainly directed to states of fugue, and civilian practice suggests that behind these there often lies a criminal act or a situation from which an immediate, even though an illusory, escape is desired. Cases occurring in war, however, indicate that other causes, such as terror, bomb blast and exhaustion, may produce not only fugues both at the time and subsequently, but also large gaps retrospectively in the patient's memory of the past.

TABLE I.—FREQUENCY OF CASES SHOWING AN AMNESIC SYNDROME IN A THOUSAND SERIAL ADMISSIONS.

	Cases admitted	Amnesia present	Frequency
Severe stress	251	87	35%
Moderate stress	155	20	13%
Trifling stress	594	37	6%
Total	1,000	144	14%

"Severe stress" means prolonged marching and fighting under heavy enemy action (e.g. in the evacuation from Dunkirk, through which the great majority of these cases passed); "moderate stress" includes experiences like periodical dive-bombing at home bases and aerodromes; "trifling stress" means the normal life of a training camp or depot, involving no greater strain than an unfamiliar life and separation from home.

In the first thousand military cases admitted to the Neurological Unit of Sutton Emergency Hospital we found no fewer than 144 in which loss of memory was a prominent

symptom. These comprise the complete series of states of fugue and retrospective losses of memory of a functional type: cases of interference with memory due to disease of the brain, and of transient loss of consciousness after head injury are not included. Severe psychological stress was an important factor in these syndromes, as will be seen from Table I.

Classified diagnostically, amnesic syndromes were found rarely in epilepsy and schizophrenia, more commonly in head injury, but predominantly in psychoneurotic states. This may be partly caused by the selective admission of psychoneurotics to our hospital. We have found only two cases of epilepsy, both showing a functional type of syndrome and not the classical post-epileptic automatism.

Fugues are a classical though uncommon manifestation of schizophrenia. Typically they represent a disturbance of consciousness in which catatonic phenomena or paranoid and hallucinatory experiences dominate the patient. But in the three schizophrenics in our material the fugue took a form superficially hysterical in appearance, and in one of them the patient had suffered from fugues since childhood. One of the others has points of interest.

Case I. (2001S): A man of 24, of psychopathic family, said he had suffered from headaches for many years and had been unhappy in the Army. After a period of leave he returned to his unit; he was worried about his wife's ill-health and a day or two later took, without permission, an Army motor-cycle to go home and visit her. On the way he had an accident in which he was not injured but £20 worth of damage was done to the cycle. He got back to his unit, but knew he was in for trouble. He began to feel dizzy, fell down, was taken to hospital mute, and when he came round two days later was unable to remember the events of the immediate past. Attempts were made without success to clear up the amnesic patch, both by hypnotism directly and under the influence of sodium amytal. But under the drug florid schizophrenic symptoms were for the first time revealed. Ever since he had joined the Army he had felt that it was a matter of general knowledge that his father had been in prison for raping a daughter and that he, the patient, was the object of public contempt on this account. He described auditory hallucinations and interference with his thinking by which his mind was made to go blank at times.

Head injury was a causative factor in ten of our cases. In half its effect was indirect; permanent impairment of the personality by cerebral trauma, with a resulting increased tendency to hysterical types of reaction, provided a basis for the operation of psychogenic stimuli months or years later. In the remainder the effect was more direct, the unconsciousness produced by concussion passing without intermission into the dissociation of a fugue. Besides the traumatic there is a constitutional factor: there was a history of neurosis or psychosis in the first-degree relatives of six of the ten patients, and in four the personality of the patient was psychopathic, even before any head injury had occurred. It was interesting to find that of the 129 psychoneurotic patients, 30, or nearly a quarter, date their amnesic disturbance from concussion or from being blown over and dazed by a bomb. This is a high proportion. In many of these cases, though subsequent treatment cleared up the major part of the amnesic period, there remained a small gap, presumably due to organic disturbance.

CONSTITUTIONAL BASIS

From Table II it will be seen that indications of constitutional inferiority were more frequent in the 32 men who broke down in the absence of any military stress than in the remainder. Nearly all (28) had fugues; three others did not actually wander off, but passed into a confused state necessitating admission to hospital, where they were found to have lost most of their memory of their past life; and one man under examination for a minor military crime lost his memory for the events on which he was being examined. In all, 6 of these 32 men showed symptoms of hysterical pseudo-dementia on admission to Sutton. Evidence of constitutional factors was strong, a positive family history and previous nervous breakdown being very common. In the families of three men a father, a mother and a sib were said to be subject to the same sort of amnesic attacks as the patient; in another a sib suffered from epilepsy. Six men had had fugues in earlier life, before entering the Army, two for the first time before puberty. Two others had suffered in earlier life from dizzy attacks and faints. In ten cases in all, fugues had occurred not once but several

times. There were similar but less frequent findings in the men who went through stress (Groups II*a* and II*b*); four of these patients had had previous fugues, and eight others had had other types of disturbance of consciousness, such as sleep-walking, hysterical fits and faints. These findings suggest the possibility of a constitutional behaviour pattern.

TABLE II.

Percentage frequency of:	Group I (32 cases)	Group II*a* (39 cases)	Group II*b* (58 cases)
(1) Family history of psychopathy	53	50	41
(2) Neurotic traits in childhood	56	65	39
(3) Poor occupational record	22	16	15
(4) Inhibited sexual life	63	40	31
(5) Poor intelligence	47	13	22
(6) Previous neurotic breakdown	42	21	14
(7) Abnormal personality make-up	50	41	35
(8) All findings 1 - 7 negative	9	21	19
(9) Hysterical traits in personality	44	22	13
(10) Obsessional traits in personality	7	14	18
(11) Malingering factor observed	23	10	5
(12) Required invaliding after treatment	72	54	53

Group I = Cases occurring in the absence of military stress.
Group II = Cases occurring under military stress. II*a* = Cases of fugue. II*b* = Cases of retrospective amnesia.

Returning to the group of men who broke down under trifling stress, one might legitimately cast some doubt on the complete sincerity and trustworthiness of all of them; but in nine of the 32 deliberate lying was observed, or there arose otherwise a strong suspicion of malingering. This, however, generally occurred in an affective setting, in which hysterical features were as a rule combined with anxiety, depression or hypochondriasis. The following case illustrates most of the features shown by Group I.

Case II. (414S): Aged 21. This man's father was discharged from the Army in 1918 with "neurasthenia". The patient could remember him wandering off on four occasions and being away for a period lasting from a day to five weeks. He never knew where he had been, and on getting home it might be another fortnight before he would or could speak. He was a moderate drinker, but of irritable sulky temper. The mother also was neurotic. The patient was nervous as a child, timid, frightened of policemen and soldiers, and in later life was unaggressive and would not strike another man back. Before the war he had thoughts of becoming a conscientious objector, and would lie awake at night in a pool of sweat thinking about it. He did not like the Army at all. For a week before his fugue he hardly slept, suffered from headaches and knew something was going to happen. On the Saturday morning he felt worse. He remembers going to the board to read Orders; he went away, felt faint, and knew nothing more until, feeling as if he were coming out of a faint, he found himself five days later outside a cinema in Barking, 74 miles away. Apart from needing a shave, he was clean and well-cared for. His mother let the hospital know that he had paid a flying visit on the evening of the Saturday of his disappearance, just dashing in and out again. In hospital he was unremarkable but was the life and soul of amateur theatricals among the soldiers, which he organized. He steadfastly refused to allow any attempt to be made to recover the memory of the five days of the fugue. He was invalided. There is, of course, a strong suspicion of malingering in this case, and it is quite likely that the exhibition of fugues by both father and son is not so much inheritance as imitation.

In the remaining 97 psychoneurotics (Groups II*a* and II*b*) who broke down under strain, the amnesic symptoms took two forms, a prolonged disturbance of consciousness, nearly always in the form of a fugue, and a retrospective forgetfulness for distressing events of the past occurring when the period of stress was over. A colleague, Dr. Denis Hill, has pointed out in private discussion an important difference between these two

types of symptom. The *fugue*, he considers, is an escape from the events of the present, a gross form of behaviour disorder, very often malingered, and shown, apart from the psychotic, as a rule only by severely psychopathic personalities. The *amnesic gap* in the memory of the past is, he thinks, a simple protective mechanism by which the continued recollection and presence in consciousness of painful events is avoided, a mechanism shown in minor degree by the normal person in everyday life. There is much to be said for this view, but the two types of manifestation cannot be so simply and certainly separated. Some of these men broke down under stress and passed into a fugue which provided them with some form of escape. Others first broke down after return to safety and passed into a fugue that served no detectable purpose. In some of the cases of retrospective amnesia breakdown had occurred at the time of stress, in others only later; in some of these the amnesia for the period of stress was diffuse and patchy, in others it was so complete and circumscribed as to resemble a fugue of the past. We have seen both fugues and retrospective amnesias in the same individual, and we have not found that the fugue is exclusively associated with grosser degrees of departure from normal behaviour. Nevertheless the figures of Table II, showing a slight but fairly consistently higher incidence of abnormal findings in the fugue cases (Group II*a*) than in the cases of retrospective amnesia (Group II*b*), indicate that the fugue is to be classed as the more abnormal manifestation. The high incidence of signs of constitutional abnormality in all groups in Table II will be noted. This is evidence against the view that the acute nervous breakdown of war is a phenomenon to which even the most normal personalities are liable. It is true that in a fifth of the acute cases of Group II no history indicating pre-existing instability was elicited. This does not mean it did not exist. A weakness of these figures is that in only occasional cases was an independent history available.

An analysis of personality traits was undertaken, but apart from two findings showed little of interest. The distribution of hysterical and of obsessional traits of personality differed sharply from expectation, the former showing a positive and the latter a negative correlation with abnormality of behaviour (see Table II). There was, however, a much more important finding which could not be conveyed in crude percentages. In examining our records we were struck by the frequency of a certain type of personality among the more normal of the men who broke down under stress (Group II). This type is best described by quotation from the records: "go-getter, energetic and active"; "sociable, fond of singing"; "high-spirited, interested in sports"; "knock-about, likes parties and jokes"; "many friends, simple type"; "high-spirited, self-confident, whisky drinker"; "rolling stone, fond of company, drinks a good deal"; "devil-may-care, likes making and taking jokes"; "generally gay, low-brow interests, exaggerated idea of own abilities". Nearly half of the patients of Group II were of this type, and they made up a very high proportion of those whose personalities were regarded as within normal limits. Summarizing, one may say that they are an outgoing type, popular with their mates, perhaps over-keen on popularity, not fond of their own company, quickly responsive emotionally but with affects tending to be shallow and lacking in persistence, not gifted with insight. The personalities classed as abnormal in Group II did not conform to the same type, showing the development, relatively to other traits, of paranoid tendencies, unsociability and poverty of energy output.

CLINICAL FEATURES

The clinical picture presented by the men who broke down under severe stress (77 of the 97 patients of Group II) frequently showed a very acute neurotic disturbance combined with a state of exhaustion resembling physical illness. This was particularly true of the earliest patients admitted after the Dunkirk evacuation. Many looked pale and drawn; others wore a blank or confused expression, and occasionally some degree of disorientation and objective confusion were seen. Headache was a prominent symptom. Symptoms of acute anxiety were not infrequently combined with others of a contradictory type, such as apathy, *belle indifférence* or even a mild euphoria. Hysterical conversion symptoms were occasionally seen, such as loss of voice, paralysis or gross tremors, even of the pill-rolling type. Physical exhaustion, as shown by a weight far below normal for the individual in question, was often present; and it is probable that this physical factor is responsible for much of the deviation from familiar neurotic pictures. The history that the patient gave was often confused, hazy and full of amnesic gaps; on other occasions

it was fairly coherent, and the suppressions of memory were only found by investigations with hypnosis or barbiturate narcosis. The following patient of Dr. Debenham's is illustrative.

Case III. (1379S): A man of 24 was admitted from Millbank Hospital, having broken down at the end of a period of leave after return from Dunkirk. He described himself later as a sociable man, fond of parties and keen on his work, but easily upset by a mistake and liable to get out of spirits. On admission he was inarticulate and it was impossible to get a connected statement from him. His head and upper trunk were constantly shaking, and he held his head bent forwards, looking out of the corners of his eyes. He muttered or mumbled to himself, or moved his lips as if in speech, but was only able to answer questions slowly and softly and with a stammer and many repetitions of words and phrases. He picked restlessly at his hands and clothes and looked round anxiously at the slightest noise. He said that a bomb had fallen near him in Belgium, and he had subsequently been much upset by the scenes of dead and dying; when speaking of the bomb tears came into his eyes. There was a suggestion of something histrionic in his behaviour. Under intravenous barbiturate he lost his inhibition, tremors and tics, and was able to give a full account of his experiences with a good deal of emotional abreaction. No one experience had upset him more than another, but he had felt deserted and helpless, harrowed by the sight of slaughtered civilians and of his own comrades being killed and, as he thought, "losing their reason". On the beach at Dunkirk he had kept a bullet in his rifle for use on himself, to save himself from being "cut up" by the Germans. After this session he was much improved; but though the retardation and apparent confusion largely disappeared for good, the tremor of the head later returned to some degree. He eventually required invaliding.

As July and August came, the post-Dunkirk cases ceased to bear this hyperacute aspect. Symptoms of physical exhaustion were more seldom seen, though the patients were still often underweight. Anxiety symptoms remained much to the fore, but the patients' complaints came to bear a more hysterical quality. These later cases have been more difficult to treat and have not done so well from the Army point of view. We sent back to duty more than half of the patients admitted in May and June, but little more than 40% of those admitted later. The following case of Dr. Craske's, admitted towards the end of July, is an example of fugues appearing comparatively late in the course of an acute neurosis.

Case IV. (1521S): A man of 24 was admitted complaining of pains in the head, giddiness, tingling feelings in the legs and hands. His mother was said to be prone to worry and depression and a brother had been nervous since the last war. After school he became an engineer, until called up from the Territorials. He married because he "had to", but the child was stillborn, and he felt cheated and has resented the loss of his freedom ever since. He described himself as a cheerful, easy-going man, a popular N.C.O., though occasionally subject to mild moods of depression. He enjoyed Army life in France, was not upset when hostilities began and at first was little affected by bombing. After a bit, however, he began to suffer from nightmares, disturbed the others by shouting in his sleep, had headaches and felt anxious and irritable. The unit was moved rapidly from place to place and they got little food or sleep. Finally the whole section of 250 men fell into an ambush and were killed or taken prisoner. He was wounded in the shoulder, and was put into an ambulance and taken to a German base hospital. He was sure that some time the Germans would kill him, and when a large number of prisoners were being moved further back, he managed to dive through a hedge and escape. He got to a farm, where he was given food and civilian clothes, and mingled with refugees. He had a number of narrow escapes from Germans and from suspicious French whom he asked for food or water; but at last he got to French occupied territory and was taken to Dunkirk hospital, where he was with a great number of other soldiers and civilians. During the evacuation from Dunkirk he was still in civilian clothes, and was repeatedly stopped and questioned; this even occurred at Margate, where he became acutely upset. He was taken to Westminster Hospital, and his wound was treated. He could do nothing but think about his experiences and cry, and could not speak to his wife when she came to see him. After leave he returned to his unit, but could not do his duties satisfactorily, and became depressed to the point of thinking of suicide.

On arrival at Sutton, he was still depressed, preoccupied with his experiences and dreaming of them at night. He said he hated the war, the Army, the sight of other soldiers. He felt completely changed, as he had always been so friendly, and now everything he did was wrong. He complained of headaches and tinglings, and was

sweaty and shaky. He told his story coherently, and there were no discrepancies or signs of an amnesic gap. In the first fortnight he made no improvement, and was then put on continuous narcosis, during which he became confused and hallucinated and talked constantly, re-living his experiences. At the end of the course of narcosis he was improved, but began to have frequent attacks of dissociation, lasting about fifteen minutes, during which he was back in France, usually seeing the Germans coming through the trees at the ambush. In the semi-hypnotic state induced by amytal further details of his history were obtained. He now related how he had been put in charge by the lad's parents of a boy in his company, and had in fact kept him under his wing. The boy was very nervous and finally in a wild panic had rushed off directly into enemy machine-gun fire, and must either have been killed or taken prisoner. A letter had now arrived at the hospital from the parents of this boy, asking for news. The patient was induced to answer the letter, and was much better, particularly when he heard a little later that his friend was now known to be a prisoner of war. But the hysterical attacks still continued, and further exploration revealed facts of a different kind. He now said that even before the offensive he had felt depressed and had had "wicked" thoughts about his wife. When he got depressed in France he got drunk, and had then several times gone with other women, feeling mean and guilty afterwards. The last time his wife visited him he had told her he did not want to see her, and he now felt he must have broken her heart. More than once after this there was improvement followed by relapse, exploration on each occasion releasing painful memories with temporary improvement. In his relapses the patient several times had fugues, one of which led to his waking up in the middle of the night in a neighbouring town; he thought he was back in France, accosted a policeman in a panic, and was taken to the station. Permanent improvement was only obtained when with much difficulty the full data of an incident in which he had deserted a wounded comrade were obtained. After this the periods of dissociation were at an end. He then had a course of modified insulin treatment with much benefit. He had a month's leave at home, and returned fit, with no recurrence of the fugues; but it was thought best to invalid him from the Army. He was clearly a severe constitutional hysteric, despite his satisfactory adaptation to ordinary peace-time life.

Several points of interest are exhibited by this case. The clinical picture shows not only hysterical symptoms, but also a fairly deep degree of depression; in the past there are corresponding foci of guilt and self-reproach, inadequately dealt with by complete suppression. The amnesic gaps were not apparent on first examination, but came out only in the course of intensive treatment; nevertheless no lasting improvement was possible until the last of the suppressed material had been brought out. Treatment had to be devoted to the physical aspect as well as to the psychological, continuous narcosis and insulin treatment playing their parts, first in dealing with the depression and agitation, finally in stabilizing recovery when attained. In this case the amnesic phenomena, which appeared first only under severe stress, were finally manifesting themselves as fugues in the most facile way, as the behaviour pattern became established.

TABLE III.—SYMPTOMS EXHIBITED BY CASES OF AMNESIA AND FUGUE PRECIPITATED BY SEVERE MILITARY STRESS.

	Amnesic group (46 cases)	Fugue group (31 cases)
Obsessional symptoms	1	—
Anxiety symptoms	38	29
Hysterical symptoms (apart from amnesia)	41	29
Depression	21	14
Hypochondriasis	20	16
Paranoid symptoms	9	2
Malingering	2	2

The association of amnesia with guilt was rare, but a prominent feature in some of our cases. Only seven men, six of them fugue cases, showed this association in the 77 who passed through severe stress. The events for which forgetfulness was so desired were for the most part the horrors and strains of that catastrophic retreat. However 43 of these

men broke down at the time of stress, thereby becoming a burden on their fellows, which might have well been a subject for uncomfortable and undesired self-examination.

A classification of the symptoms shown by the men who came through severe stress is attempted in Table III. Anxiety and hysterical manifestations were the most prominent symptoms, though conversion symptoms were uncommon. Symptoms resembling those of schizophrenic states were very rare, hallucinations and catatonic-like behaviour being seen in one case each. Malingering also was rare.

TREATMENT

The treatment of these states is, of course, the treatment of the patient as a whole. But we have found it best not to ignore the amnesic symptoms, to explore the gaps in memory, and to be on the look-out for them, even when they are not immediately obvious, or are denied. These patients can certainly get well without interference; but men admitted to us months after return from Dunkirk have seemed to benefit from the restoration of lost memories, from which they had suffered throughout the intervening period. The better the personality, the more is the lack of knowledge of what happened in an amnesic period a source of worry to the patient. The method of exploration is a matter of personal choice; but we have found in our unit that the administration of an intravenous barbiturate is of particular value in these acute patients, who are often rather insusceptible to direct hypnosis. Under the drug it is easier to establish a semi-hypnotic contact, a point of value to the doctor who is uncertain of his hypnotic powers. The information gained will often be a mixture of truth and fantasy, and will have to be sifted. In any case the process is only one of the steps in treatment, the next being an emotional synthesis, the restoration of normal physical good health, and the readaptation of the patient. When symptomatic recovery is attained, reconditioning should begin. For the best results the patient should be convinced by actual trial that he can face the duties he carried out before breakdown. Unfortunately this is not possible in the hospital framework, so that chances of relapse are difficult to estimate. It is here that rehabilitation centres would have one of their main functions.

The progress of these neurotic states would in the uncomplicated case normally be back towards the patient's natural base-line, whether that is one of good or ill health. Unfortunately in this interim stage in the war the complicating factors are many. The patients of Group I are largely a constitutionally inferior material, and only a partially satisfactory adaptation could be expected. But it was disappointing to find so many of the more normal personalities of Group II incapable of being brought to the point of facing renewed military duties, even in the less risky circumstances of service at home. It was here that the lack of rehabilitation camps under combined psychiatric supervision and military discipline made itself felt. Even of those whom we did send back to duty about half have had subsequently to be invalided at some other centre. So far as we have knowledge of the invalided patients, they are nearly all at civilian work, but many still suffer from anxiety symptoms in air-raids. The difficulty is that we have not as yet been able to tackle the pathogenic situation, that of the war, which awaits, not psychotherapy, but curative surgery.

SUMMARY

In a complete series of a thousand military neurotic casualties there was found the high number of 144 who presented an amnesic syndrome. The frequency was much the highest in those cases who had undergone severe stress, such as the Flanders retreat. Epileptics, schizophrenics and cases of head injury were seen, but the great majority were psychoneurotic. In about a quarter of these cases trivial concussion or dazing seemed to have played a precipitating rôle in producing states of hysterical dissociation. Those who broke down in the absence of stress were for the most part severe psychopaths, and included many cases of malingering in an affective setting. In 83% of all the psychoneurotic cases there were indications of constitutional instability. Some evidence was obtained that there may be a specific constitutional tendency to fugues and other forms of disorders of consciousness. In cases occurring under stress the amnesic syndrome showed two main manifestations, fugue and retrospective gaps in the memory of past stress. Evidence tended

to show that patients developing fugues had more psychopathic traits than those who showed only a retrospective amnesia. Patients breaking down under stress were, with striking frequency, men of a simple, superficially well-adapted, extraverted type of personality. The amnesic symptoms were shown in a setting in which affective features were prominent; these were, in descending order of frequency, anxiety, hypochondriasis, depression and paranoid symptoms. The treatment and prognosis of these cases are discussed.

Section of Urology

President—T. E. HAMMOND, F.R.C.S.

[*June* 26, 1941]

CASES

Three Cases illustrating Result of Author's Operation for Urinary Incontinence.—TERENCE MILLIN, F.R.C.S.

It is now more than two and a half years since I first described my operation for the relief of urinary incontinence to this Section (*Proceedings*, 1939, 32, 777; Sect. Urol., 31). It consisted in lapping the corpus spongiosum as close as possible to the membranous urethra with three turns of 5/8 in. chromicized ribbon catgut. At that time several members expressed themselves sceptical as to the permanence of the results and others forecast stricture formation. These three cases to-day disprove these criticisms. One of the patients was operated upon six years ago. The operation is simple of execution, taking but ten to fifteen minutes to perform, and gives results far exceeding any other procedure yet described, not excluding the gracilis operation.

Some few months after I read my paper Mr. Bernard Ward employed the procedure in a case where incontinence of both urine and fæces were present as a congenital abnormality. He tells me that his case, now some two years later, presents a highly successful result.

The successful case described by Dr. Bentley Squier of New York many years ago (1911) in which he made a muscle sling by suturing the remnants of bulbo-cavernosus to levatores ani proved to be a complete failure a year later. Dr. Squier has asked that this information be put on record.

During the past six years I have operated upon 10 such cases of urinary incontinence in the male and in 9 the result is excellent. The one failure was due to the catheter slipping out the first post-operative night and the accident not being discovered until some hours later. Some difficulty was experienced in reintroducing a catheter; a temporary fistula developed with sepsis. The fistula closed spontaneously but the urinary control was not improved. I propose reoperating upon this case.

Case I.—H. W., aged 79. *History.*—Suprapubic prostatectomy elsewhere 1938; complete incontinence day and night since operation.

Examination (March 1940).—Uriniferous smell with underclothes soaking. C.N.S., abdominal and rectal examination negative; catheter passed with ease, only few drops of urine being withdrawn. Cysto-urethroscopy revealed no abnormality in bladder or urethra beyond a widely-open vesical outlet and lack of tone of compressor urethræ.

Operation (April 1940).—Ribbon catgut technique under continuous pentothal. No. 10 E. rubber catheter stitched in urethra. (Operation time 12 minutes.) Catheter removed tenth post-operative day. Discharged sixteenth day with control almost but not quite complete. Complete control not established for several weeks.

Result.—Complete control fourteen months after operation. Can hold urine for six hours during the day; disturbed once at night. Never the slightest leakage. Urinary stream excellent; no instrumentation since discharge from hospital.

Case II.—W. P., aged 61. *History.*—Suprapubic prostatectomy elsewhere August—September 1933. Control following operation remained very imperfect though not wholly incontinent. Compelled to wear incontinence bag during the day and keep penis in urinal at night; could at times void 3-4 oz.

Examination (July 1934).—No improvement in urinary control in nine months since operation. C.N.S., abdominal and rectal examination negative. Urine mildly infected. Cysto-urethroscopy revealed small nodule on right side of vesical outlet and poor tone of compressor urethræ.

Operation (July 1934).—Suprapubic excision of adenomatous nodule at vesical outlet. Result: No improvement in urinary control.

Operation (July 1935).—Ribbon catgut operation under spinal anæsthesia (first case). No. 10 E. gum-elastic catheter in urethra for seven days. Discharged from hospital on fourteenth day with almost complete control.

Result.—Complete control six years after ribbon catgut operation. Urinary stream excellent. 12/15 Liston steel passed easily October 1939, four years after operation.

Case III.—A. C. H., aged 62. *History.*—Harris prostatectomy combined with diathermic coagulation of small papilloma, September 1935. Uninterrupted convalescence. Within first month after discharge from hospital, several attacks of retention necessitating catheterization. Returned to hospital where punch resection of contracted prostatic urethra was carried out. Partial incontinence developed. Light clamp used by day and urinal at night. No improvement after three years, despite intermittent dilatations with Kollmann dilator.

Examination (January 1939).—C.N.S., abdominal and rectal examination negative. Urine uninfected; no residuum. Cysto-urethroscopy negative except for loss of tone of compressor urethræ; no narrowing of prostatic urethra.

Operation (January 1939).—Ribbon catgut technique under gas-oxygen. Catheter removed eighth day. Discharged thirteenth day with full control.

Result.—Control virtually complete two and a half years after operation. Very occasionally when rising from sitting posture, if bladder is full, a few drops of urine escape. Urinary stream full; no urinary frequency. Bi-annual dilatations employed lest recontracture of prostatic urethra occur.

SPECIMENS

Bladder Diverticulum and Enlarged Prostate.—H. P. Winsbury-White, F.R.C.S.

The excised sac is about 2 in. deep and the prostate shows a middle lobe enlargement.

History.—F. C. J., aged 57, complained of frequent and difficult micturition and some thirst. Symptoms had been getting worse over a period of several months. The difficulty was such that he could only pass water after putting his foot up on to the seat of a chair.

On examination the patient was thin and of good colour. The bladder was visibly distending the abdomen to the umbilicus, the tongue was clean and moist, rectal examination showed a slightly enlarged prostate.

Urine: Clear; no pathological elements. Blood urea was 55 mg. per 100 c.c.

Treatment.—The patient was admitted to hospital and gradual decompression carried out through an indwelling catheter. There was slight hæmaturia as a result of this. Suprapubic cystostomy was performed in due course, and a diverticulum situated near the right side of the bladder base and an enlarged middle lobe of the prostate were discovered. Because of the necessity to remove both the diverticulum and the prostate, it was considered advisable to drain the bladder suprapubically for a period before carrying out these operations.

Three weeks later diverticulectomy and prostatectomy were carried out. The patient made a satisfactory recovery. When last seen, three months after the second operation, there was no residual urine and the patient was passing his water freely.

Comment.—When a diverticulum is present at the base of the bladder it is almost constantly associated with a bladder-neck obstruction. The latter will require to be removed as well as the sac.

As far as the actual operation is concerned it is important to provide adequate drainage for the pelvic floor outside of the bladder after the diverticulum is removed. In this case the drainage provided was a long strip of corrugated rubber 2 in. wide going down to the most dependent part of the pelvis and was not disturbed for one week. After this period the drain was quickly shortened. This method proved highly satisfactory.

In answer to a question about the necessity for doing the operation in two stages, Mr. Winsbury-White replied that in his experience when it was necessary to remove the prostate as well as a diverticulum, the patient stood the ordeal better in two stages than in one stage; this was in spite of the added difficulty for the surgeon, from the preliminary cystostomy.

Carcinoma of the Colon Invading the Bladder Wall.—F. McG. Loughnane, F.R.C.S.

Mrs. K., aged 66. *History.*—Admitted to hospital 4.3.40 complaining of hæmaturia. There was very little bladder pain, and no other symptoms.

Examination.—Cystoscopy showed a large growth at the fundus of the bladder, which was diagnosed malignant.

Operation.—On exposure of the bladder a large lump was felt, so the peritoneum was deliberately opened. The lump was found to involve both bladder and sigmoid. The uterus was free and there were no palpable glands. The sigmoid was divided and the affected portion along with part of the bladder was removed. The divided ends of the bowel were ligated and invaginated, and a side-to-side anastomosis performed. The bladder was stitched up and a drainage tube left in.

Result.—The patient seemed to be progressing well, but on the seventh day suddenly collapsed and died. Convalescence had been afebrile, the bowels had acted, and urine drained freely. Unfortunately no post-mortem was allowed.

Pathological report: Alveolar columnar-celled carcinoma of the colon invading the bladder wall.

Comment.—There are two interesting features about this case: First, the absence of any bowel symptoms, and second, despite the size of the invading growth, the absence of a vesico-colic fistula.

Five-Year-Old Hypernephroma.—Alex. E. Roche, F.R.C.S.

History.—The patient, then aged 14, was seen in February 1935 at the West London Hospital, because of occasional recent hæmaturia. There was a history of trauma to the left loin about ten months previously, two boys at school having fallen on him. Hæmaturia had occurred only subsequently.

Examination.—Abdominal examination was negative, and the urine (from memory—notes mislaid) contained a few red cells, pus cells, and staphylococci.

X-ray pictures (19.2.35) gave the appearance of a round calcified mass at the upper pole of the left kidney, and uroselectan films (25.2.35) showed distortion and depression of the left pyelogram. The radiologist reported: "Left kidney distorted by cyst in upper pole." Again from memory, there was no evidence of tubercle or hydatid disease.

Subsequent history.—Because of the history of trauma and the age of the patient (an unusual one for neoplasm) I diagnosed calcified hæmatoma in connexion with the upper left renal pole, and, as the patient seemed quite well and was symptomless at the time, advised waiting a little, and exploring him if hæmaturia recurred.

I lost sight of the patient until he returned to hospital in July 1940, then aged 19. He complained of two days' aching pain in the left loin (he had had recurring pain) and of hæmaturia, which he had had about two or three times a year.

Examination.—The urine, apart from a little blood, was normal, and cystoscopy showed yellow urine and a normal bladder, except for multiple submucous hæmorrhages.

His blood picture proved normal. At X-ray examination (1 and 5.8.40) I recognized the calcified mass, and thus the patient. The mass was depressing the left kidney, and had

obviously grown quicker than the patient himself, and was bulging outwards his lower left ribs. An X-ray picture of his chest showed no evidence of secondaries.

Operation.—On September 5, 1940, I performed left paramedian transperitoneal nephrectomy, with a long lateral cut. The mass was large and heavy, and was separated from the suprarenal. A firm mobile gland, of walnut size, antero-internal to the renal vein, was also removed; but a small clump of tiny, shotty, hard glands on the aorta was left alone.

Section of the mass showed a large globular hypernephroma, with some normal kidney tissue below. Microscopy of the kidney mass and of the gland both showed the appearances of hypernephroma.

The patient has had deep X-ray therapy, and appeared well when seen at hospital, nine and three-quarter months after operation.

Left calcified hypernephroma (1.8.40).

Comment.—Interesting points in the case are: (1) The unusual age of the patient, hypernephroma usually affecting much older patients; (2) the known duration of the growth for at least five and a half years; (3) the comparatively low malignancy, in that, although a neighbouring lymph gland was replaced by growth, there was no evidence of chest or other secondaries; (4) the extensive calcification of the growth. Contrary to what one might imagine, calcification of renal growths has been claimed as a sign of extra malignancy, for instance, by Wesson and Ruggles in their "Urological Roentgenology", where, speaking of hypernephroma they state: "The presence of extensive calcification is of great importance from the standpoint of prognosis. It is present only with a very malignant type of tumour."

However, this case proves that calcification may co-exist with low malignancy. I should like to hear opinions on this point—whether calcification is a sign of added malignancy or whether, as one might have thought, it may signify chronicity and thus low malignancy.

(The opinions expressed favoured the latter alternative.)

Unusual Foreign Body in Urinary Bladder.—J. GABE, F.R.C.S.

Description.—The specimen is a Kirby hair-grip removed from the bladder of a girl of 16 years. It is encrusted with phosphates at one end.

Clinical notes.—A. H. was admitted to St. Andrew's Hospital, Bow, in March 1938 with three months' history of dysuria, frequency and lower abdominal pain, followed by urinary incontinence. She was a thin, shy girl with many lesions of acne vulgaris on her face. Apart from this no abnormality could be found on physical examination.

Investigations.—Urine contained pus and various organisms. *Radiograph* of the pelvis revealed a foreign body, which appeared to be in the bladder. *Cystoscopy* was impossible as the bladder held very little fluid. An attempt to remove the foreign body *per urethram* failed.

Operation.—Suprapubic cystotomy.

Convalescence was normal.

No information could be obtained as to how the hair-grip came to enter the bladder. It was probably introduced by the girl herself.

Impacted Ureteric Calculi.—J. GABE, F.R.C.S.

Description of specimens.—Two calculi removed at operation from a man of 30 years. They were lying in the much-dilated pelvic portion of the ureter, close to the bladder.

The larger calculus: This is rather egg-shaped with the upper end much flattened. It has a rough surface and is heavy, weighing 48 g. It is 4 cm. across from side to side and from above downwards. It consists chiefly of calcium phosphate with traces of calcium oxalate.

The smaller calculus: This is faceted on its upper surface, where it was in contact with the larger stone, and is semilunar in shape. It lay nearer the bladder.

Clinical notes.—W. G. H. was admitted to St. Alfege's Hospital, Greenwich, in December 1940 with a two years' history of intermittent pain in the right loin. Attacks recurred every two to four weeks. There were no other symptoms.

Clinical examination.—Healthy appearance, robust physique. No abnormal signs in urinary tract.

Investigations.—Catheter urine grew *Staph. albus.*

Excretion urography: Marked right hydronephrosis. Normal left pyelogram. Large calculus in lower end of right ureter with small calculus below it. *Cystoscopy*: Bulge above right ureteric orifice; no efflux from that side; left normal, clear effluxes. Bladder normal. Ureteric bougie arrested just beyond right ureteric orifice. *Urea clearance test*: Blood urea 28 mg.%. Blood urea clearance (standard) 60 c.c. per minute (111% of average normal).

Operation.—Right nephro-ureterectomy, first by a lumbar and then by a mid-line suprapubic incision. The kidney was markedly hydronephrotic. The ureter was dilated throughout its length. The pelvic portion was the widest, measuring nearly 5 cm. across. Below the stones, and between them and the bladder, the ureter was hardly dilated at all.

The patient made an uneventful recovery.

Histological reports (Dr. E. N. Allott): (1) *Kidney*: Shows hydronephrosis, but no evidence of ascending infection. (2) *Ureter*: (*a*) *In the region of the stones* shows loss of epithelium, the surface consisting of granulation tissue containing numerous blood-vessels; (*b*) *below the stones* the ureter is apparently normal in structure.

I desire to express my thanks to the Medical Superintendents of the above-named hospitals, Mr. J. R. M. Whigham and Dr. B. A. Young respectively, and to Dr. W. A. Daley, Medical Officer of Health, for their kind permission to show these specimens.

Renal Specimens.—R. H. O. B. ROBINSON, F.R.C.S.

(1) **Renal tumour** (Wilms), removed from a male infant aged 15 months. History of three months' abdominal swelling. Pyelograms showed some secretion. Course of pre-operative X-rays produced no demonstrable diminution in the size of the tumour. Trans-peritoneal nephrectomy. Now, six months later, child appears very well. Tumour weighed 2 lb. and macroscopically resembled a fibrosarcoma, a surprising amount of normal renal tissue being present. Microscopically the appearances were typical of a Wilms' tumour.

(2) **Renal cyst.** Large pseudocyst, the size of a grapefruit, from the upper pole of the kidney. The patient, aged 70, had had a nephrolithotomy many years previously. Clinical signs suggested hydronephrosis but intravenous pyelography revealed the correct diagnosis. The condition was due to occlusion of the calix with cyst formation.

New Collecting Apparatus for Cutaneous Ureterostomy.—TERENCE MILLIN, F.R.C.S.

This new type of collecting apparatus for use in cases of cutaneous ureterostomy is a modification of my bag devised several years ago for suprapubic cystostomy. Its advantages seem apparent and it has been successfully employed in several cases. It has been made for me by Mr. Donald Rose.

Case example: Following a complete nephro-ureterectomy for tuberculous disease in October 1937, progressive vesical ulceration leading to intolerant systolic bladder with false incontinence and finally a pyonephrosis with frequent rigors, pyrexia, &c., demanded a urinary deviation. Owing to poor general condition at the time, transplantation of the solitary dilated ureter into the colon was not deemed safe and cutaneous ureterostomy was carried out in September 1939. Since January 1940 the patient, a busy medical practitioner, aged 47, has been back at full work. No urinary leakage ever occurs. The catheter passes 7½ in. along the ureter before entering the renal pelvis. The catheter, having terminal and lateral eyes, is removed once weekly, washed and boiled, and replaced. No pelvic lavage is employed. Complete comfort is experienced.

Section of Neurology

President—GEOFFREY JEFFERSON, M.S.

[*May* 15, 1941]

A Form of Visual Disorientation Resulting from Lesions of the Right Cerebral Hemisphere

By W. RUSSELL BRAIN

MUCH of our knowledge of visual disorientation is derived from the study of cases of gunshot wound of the brain during the last war, especially by Riddoch (1917) and Holmes (1918, 1919). Riddoch (1917) in his paper on the effect of occipital injuries reported a case, No. 3 in his series, of a patient who was unable to localize an object seen, to tell which of two objects was the nearer to him and to appreciate visually depth and thickness in objects, notwithstanding perfect consciousness of light and shade and possession of binocular vision. Holmes (1918) reported a group of six cases of visual disorientation and later (1919) summarized the abnormalities observed in eight cases. Though the clinical picture differed somewhat in different cases the cardinal features of the patients in this group were as follows: (1) There was a disorder of absolute localization of objects seen, leading to an inability to touch them or indicate their position correctly. (2) Relative localization was also impaired so that the patient was unable to say which was the nearer of two objects. (3) The patient was unable to determine the relative lengths of two lines or the relative sizes of two objects. (4) Walking revealed a gross disorder in spatial orientation. Patients would run into objects which they clearly saw, and have great difficulty in finding their way about and in learning the topography of the room. For example, a patient intending to go to his bed would see where it was but set out in the wrong direction. In some cases topographical memory for experiences which occurred before the injury was defective. One patient was unable to describe routes previously familiar to him. Memory for objects, however, was preserved. (5) There were difficulties in picking out objects visually and in counting them, and also in reading. (6) Recognition of movement in a sagittal plane, i.e. to and fro, was defective, but lateral movement was recognized. (7) Visual attention was impaired. (8) Various disorders of the ocular movements were observed. (9) In one case only was stereoscopic vision lost (Holmes and Horrax, 1919). In all Holmes' six cases both cerebral hemispheres were injured. He stated that he had not seen similar symptoms produced by unilateral lesions and that "it may be assumed that bilateral lesions are necessary for their appearance". The lesions responsible for the symptoms were localized in the posterior and upper parts of both parietal lobes. In the two cases in which post-mortem examinations were obtained the lateral lesions involved the angular and supramarginal gyri, while the mesial were placed immediately dorsal or posterior to the splenium.

Riddoch (1935), however, reported two patients in whom visual disorientation, limited to the right homonymous half-fields, was caused by a tumour in the left parietal region.

Kleist (1922) in his review of war injuries of the brain adds nothing to the symptoms of visual disorientation, and is mainly concerned with its classification as also are more recent reviews by Quensel (1931) and Lange (1936). Pötzl (1928) contributes an interesting psycho-physiological analysis to which allusion will be made later.

This paper is an account of three cases of a distinct form of visual disorientation resulting from a lesion of the posterior half of the right cerebral hemisphere and characterized by an inattention to the left half of external space, causing a tendency to turn to the right instead of the left in walking. The distinctiveness of this form of visual disorientation and its relationship to a lesion of the right cerebral hemisphere do not seem to have been fully recognized before, though I have been able to find a few examples, variously described, in the literature.

REPORTS OF CASES

Case I.—Male, aged 47. Glioblastoma multiforme of right parieto-occipital region verified at operation.

History.—In August 1939 he began to bump into things on the left side. The left hand became clumsy and he began to suffer from headaches. His wife noticed that his temperament had changed and that he had become irritable. During air-raid warnings he got lost in his room, tried to put his dressing gown on upside down and was unable to knot his tie. He then had left homonymous hemianopia, over-reaction to pin-prick over the left upper limb and gross impairment of postural sensibility in the left fingers and toes. On September 30, 1939, he was operated upon by Mr. P. B. Ascroft who exposed a glioblastoma multiforme in the right occipito-parietal region, the section of which showed large numbers of fibrillary astrocytes and also areas of less differentiated cells. He improved remarkably after operation and had a course of deep X-ray therapy. During the early summer of 1940 there was increasing weakness of the left upper and lower limbs and vision to the left side deteriorated again. Headache, of which he had never been completely free, increased in severity. There was occasional vomiting and hiccup was troublesome.

Disorders of orientation.—During this time he had experienced difficulty in finding his way about. This occurred in daylight, but was worse in the dark. In going from his bedroom on the first floor downstairs to the sitting-room he tended to turn to the right instead of to the left and in consequence would arrive in the dining-room. He then recognized his mistake and this caused him irritation. He experienced no difficulty in visualizing the correct route. He found it difficult also to find the electric light switch above his head in the dark, although he could picture where it ought to be. He had great difficulty in putting on his clothes. He said that it was quite hopeless for him to try to put them on in an automatic fashion. He could put on his pyjama coat only if he laid it out first on the bed. He had learned that the handkerchief pocket was on the left side and the buttons on the right side and by utilizing these landmarks he was able to put it on. If he tried otherwise he got in a complete muddle.

Awareness of left side of the body.—He complained that he did not know where the left side of his body was. He might awaken lying on his left arm and not know where it was and when eating he would hold the fork up in the air without knowing it. He said that the left side of his body felt different from the right side and as if it were on the right side. This was a very peculiar feeling and he could not describe it properly. It was especially marked in the left middle and ring fingers. He said: "When I do anything with that hand I feel as if I ought to be using the right hand."

Examination.—July 9, 1940: Right-handed man, intelligent and co-operative. No aphasia. No disturbance of speech or writing. No apraxia. No disorder of recognition of objects.

Fundi normal. Left homonymous hemianopia. Slight weakness of left lower face. Spastic weakness of left upper and lower limbs, more pronounced in the lower than the upper, with increased tendon reflexes and diminished abdominal reflexes on the left side. Plantar reflexes flexor. Sensibility: relative anæsthesia to light touch on the left half of the body, but touches when felt were accurately localized. Relative left hemi-analgesia, gross postural loss in the left fingers and toes, inability to recognize an object placed in the left hand and no threshold for tactile discrimination on the left hand. He was able to recognize his own and the observer's right and left hands and identify fingers named on his own and the observer's hands. A further course of X-ray treatment caused temporary improvement, but after a few months he deteriorated again and became completely disorientated.

Case II.—Female, aged 47. Hypertension: Cerebral hæmorrhage into posterior half of right cerebral hemisphere verified by autopsy.

History.—On July 11, 1940, she was walking along the pavement in which a hydrant standard was standing in a hole. She did not see it and caught her foot in the hole, falling and striking her right lower abdomen on the top of the hydrant. She did not think she hit her head nor was she unconscious. She was helped home by a workman and immediately developed severe headaches and photophobia and remained in a state

of semi-consciousness and mental confusion with headache and vomiting for two or three days. She was then sent into the New End Hospital, Hampstead, where she stayed for a week and was then discharged as she wanted to go home.

Visual disorientation.—On her return home she did not always recognize her room and it was noticed that she could not find her way about the flat. When she set out for the bathroom she arrived at the lavatory, which was a door on the right, and when she tried to go to the lavatory she made a similar mistake, took a turning to the right and got lost again. Yet when she was asked how she would find her way to the bathroom, the door of which was on the left at right angles outside her bedroom door, she replied: "I should go first to the cupboard in which my husband keeps his clothes." (This was near the bedroom door.) "Then I should open the bedroom door and outside would be where the coats are hung up. I should then look for the electric light switch which is outside the bathroom, because the Borough Council won't allow it inside, and I should then find the bathroom and the bath would be in it." Thus she clearly visualized the landmarks of the correct route. When asked to describe how she would find her way from the tube station to her flat she described this in detail correctly and apparently visualizing the landmarks, but she consistently said right instead of left for the turnings except on one occasion. When offered objects she tended to pass point to the right with both hands.

Examination.—August 1, 1940: Right-handed. Co-operative. Slightly retarded mentally. Speech: She understood all that was said to her and was able to speak and read correctly except for occasional verbal mistakes. No agraphia. Fundi normal. Left homonymous hemianopia. Pupils and ocular movements normal. Slight weakness of left side of face, and left upper and lower limbs which were markedly hypotonic, Slight motor apraxia in left upper limbs. No inco-ordination. Arm-jerks sluggish and equal; abdominal reflexes brisker on the right than the left side. Knee-jerks absent; ankle-jerks, left brisker than right. Plantars flexor. Sensibility: No cutaneous anæsthesia. ? slight analgesia to pin-prick over left upper limb. Appreciation of passive movement of the fingers and toes slightly impaired on the left side.

Distinction of right and left.—She was able to name her own and the observer's right and left hands, fingers and feet with only occasional mistakes. She tended on one occasion, however, to move the right arm when asked to move the left. When asked to touch her own nose and the observer's finger alternately she several times became confused between her own and the observer's nose. She lived for nine weeks after the onset of her illness and during the latter part of that time she was completely disorientated. Blood-pressure 210/150.

Post-mortem examination by Dr. J. Davidson showed an old cerebral hæmorrhage in the right hemisphere. It extended from the vicinity of the occipital pole to halfway between that and the frontal pole. The area was occupied with pale red blood-clot. The hæmorrhage had apparently arisen from the rupture of an atheromatous vessel.

Case III.—E. Y., left-handed male, aged 53. Abcess of right parieto-occipital region secondary to bronchiectasis, verified at operation.

History.—In July 1940 he complained of cough, sweats, loss of weight and hæmoptysis since an attack of influenza the previous winter. X-ray examination of the chest showed a shadow in the right middle lobe near the hilum. Bronchoscopy and radiography after lipiodol injection showed bronchiectasis.

On March 2, 1941, he had a convulsion. He was standing just outside his house and feeling funny went indoors. He then became confused, felt "in the middle of a sort of maze", did not know where he was nor what to do and lost consciousness and fell. He became cyanosed, twitched on both sides of the body and foamed at the mouth. He was unconscious for fifteen minutes and semiconscious for half to three-quarters of an hour. He fractured his right clavicle in his fall.

After recovering consciousness speech was slow and hesitant. In reading he would miss out words and showed a tendency to read words from right to left, trying to pronounce "of" "fo" for example. When given coffee on his right hand and bread on his left he took up the bread and tried to drink it. He tried to eat an egg like an apple, putting the shell into his mouth. He was unable to fill his pipe. During the next week he suffered from headaches of increasing severity, vomited once and was sometimes drowsy.

Visual disorientation.—To go from his bedroom into his sitting-room involved crossing the hall and entering the left hand of two doors facing him. The door to the right led into the drawing-room. In trying to do this he went into the drawing-room, but at once recognized his mistake and became irritated by it. On returning to his bedroom

in which there were two beds placed head to foot facing him he got into the right hand one instead of the left which was his own bed. His wife had noticed his tendency to go to the right in walking. There was no disorientation in pointing with his eyes closed to objects on either side which he had previously been allowed to see, nor in grasping objects. He identified his own and the observer's right and left hands correctly after a little hesitation.

Examination.—March 12, 1941: He was left-handed as a child, and still used his left hand for cutting bread and dealing cards, but wrote with his right hand. Alert and co-operative, and orientated in place and time. Spontaneous speech was slightly hesitant, but otherwise normal. In reading, words were omitted and there was paraphasia. He said he felt an impulse to read from right to left. He wrote his name correctly, but when asked to write "God Save the King" there was paragraphia. He understood spoken speech and named objects correctly. He used common objects correctly, but when asked to carry out more complex actions there was severe ideational apraxia. The optic discs were normal. There was visual inattention in the left half-fields. Though the fields appeared full, perception of movement was defective in the left half-fields, and two days later there was a left homonymous hemianopia. At first the only other abnormality was a relative exaggeration of the tendon reflexes and diminution of the abdominal reflexes on the left side, but two days later there was a hemiparesis with impairment of postural sensibility on the left side and astereognosis in the left hand.

On March 15 Mr. Northfield operated and found an abscess fairly near the surface through a burr-hole just below and behind the right parietal eminence. There was no capsule and the brain was extremely soft. He removed 10 c.c. of thick pus. A second aspiration was made three days later and the patient is now free from all symptoms and signs except occasional headaches.

THE NATURE OF THE VISUAL DISORIENTATION

All three patients, then, with a massive lesion of the right parieto-occipital region, exhibited visual disorientation. Two degrees of this can be recognized in each case. In its less severe and more selective form it consisted of a disorder of route-finding. Owing to a tendency to turn to the right instead of to the left the patients lost their way in familiar surroundings. In its more severe manifestations, present in the early and late stages of No. 2's illness, and the end of No. 1's and as the aura of the epileptic attack which initiated No. 3's, there was complete disorientation as to place so that the patients did not recognize their surroundings. All three patients showed some defect of postural sensibility on the left side. Negatively they exhibited no loss of topographical memory, no defect of judgment of absolute or relative distances as far as this could be tested, except that No. 2 tended to pass point to the right with either hand when trying to grasp objects, no gross difficulty in recognizing their own or the observer's right and left sides, and no visual agnosia for objects. One patient, No. 1, had the greatest difficulty in dressing himself, but the other two always had this done for them.

I have been able to find a few similar cases in the literature, though the nature of the disorder of route-finding does not seem to have been fully recognized. Hughlings Jackson (1876) reported a case of tumour of the right temporo-occipital region causing left hemiplegia and "imperception". The patient, though her topographical memory was well preserved, got lost in familiar surroundings and made mistakes in dressing herself. Wendenburg (1909) described a case of tumour of the right occipital lobe in a man whose first symptom was inability to find his way about, and who also had great difficulty in dressing himself. Finally he became completely disorientated in space. In two cases, (Wilbrand, 1892, and Pötzl, 1928), the syndrome was complicated by concomitant lesions of the left hemisphere but in Pötzl's case the left hemisphere lesion was relatively unimportant and the case is interesting on account of his inferences from it.

It is clear that the disorientation cannot be attributed either to visual inattention or to hemianopia in the left half-fields. Patients with hemianopia may run into objects, but they do not get lost in their own homes. Evidently we have to do with a disturbance of the complex function of spatial orientation and not with a mere inability to see normally. As Holmes pointed out in connexion with his cases, the patients are more disabled than a blind man, who can still find his way in familiar surroundings. It is also clear that the disorder is not due to a loss of topographical memory nor to a visual

agnosia which made it impossible to recognize the surroundings, for though this developed in the severe stages, it was not present in the milder ones when patients who arrived at the wrong room recognized that they had made a mistake.

Pötzl concluded from his patient that the essential disturbance was a disorder of orientation in surrounding space from an error of discrimination of right and left turning. The clinical picture in his case was confused by the effects of the left hemisphere lesion, but in essence he is right, though we must add that the effect of a lesion of the posterior part of the right hemisphere is to cause the patient to neglect the left half of external space and to select a right instead of a left turning in error. This mistake extended even to No. 2's verbal description of her route from the Underground Station to her home. It is highly significant that No. 1 in whom sensibility, especially postural sensibility, on the left side of the body was most profoundly affected had a similar feeling about his body. He said that the left side of his body felt as if it were on the right side and " when I do anything with that hand I feel as if I ought to be using the right hand ". No. 2 when asked to move the left hand tended to move the right. Obviously the relationship between one half of the body and the corresponding half of external space is intimate and complex: we should expect their perceptual disorders to be equally closely related. It is only a short step from No. 1's feeling about the left half of the body to an actual imperception of hemiplegia. We should not be surprised, therefore, if cases occur in which the patient is unaware both of the left half of external space and of the left half of his body. Through the kindness of Dr. Parkes Weber I have recently seen a case of this kind. Owing to multiple cerebral emboli the patient was completely blind and had left hemiplegia. He exhibited anosognosia for both his blindness and his hemiplegia. Though he heard sounds with his left ear they were referred to the right half of external space. As Pötzl (1928) points out, the right hand is primarily related to the right half of space and the left hand to the left half. One might add that the right half of the body usually lies within the right half of the visual fields and the left in the left half. Hence, as Pötzl (1924) suggests, awareness of space and its three dimensions appears to be a special function of the parietal lobes. From the visual cortex is derived the perception of external space and the localization, in part, of visual objects, especially in a coronal plane. From the postcentral convolution comes awareness of the body posture. A reciprocal relation between these two sensory fields through the parietal association paths is the basis of awareness of the relationship between the body and external space.

CONCLUSION

This form of visual disorientation is an inattention to, or temporary agnosia for, the left half of external space. Thus it differs from a failure to appreciate visually the relative and absolute distances of objects, which is an agnosia for spatial relationships within a space of which in itself the patient is normally aware. This distinction is fully discussed elsewhere (Brain, 1941). Disorientation in walking is secondary to the neglect of the left half of space. The integration of the two vertical halves of visual space into a single whole is so important that the complete disorganization of this function by serious damage to the right parietal lobe leads to complete disorientation in space.

Similarly the apraxia for dressing seems to be the outcome of disordered recognition of the spatial qualities of clothes, especially perhaps the discrimination of their right and left sides. This symptom is not peculiar to lesions of the right hemisphere. I have recently seen it associated with visual disorientation in the right half-fields, in a patient of Mr. Northfield's who had a traumatic lesion of the left parieto-occipital region.

It will have been noted that in my third patient who was left-handed, although apraxia, alexia and agraphia were added to the picture, the form of spatial disorientation was unchanged, which suggests that in respect of the dominant hemisphere the organization of space perception is not linked with speech.

Finally it may be asked why this form of visual disorientation seems to occur only as a result of lesions of the right hemisphere, and why no cases have been described of left hemisphere lesions causing a tendency to neglect the right half of space in the same way. I shall not attempt to answer this question here, but will only draw attention to the fact pointed out by Barkman (1925) that in all reported cases of imperception of hemiplegia the hemiplegia has been on the left side.

SUMMARY

(1) Three cases are reported of a form of visual disorientation resulting from lesions of the parieto-occipital region of the right cerebral hemisphere.

(2) In its less severe degrees this is characterized by a neglect of or inattention to the left half of external space leading to disorientation of walking. In its more severe degrees there is complete disorientation in space.

(3) Difficulty in dressing may also be observed.

(4) The relationship of this to other forms of visual disorientation and also to imperception of hemiplegia is discussed.

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The Clinical Significance of the Pattern of Cutaneous Innervation

By G. WEDDELL

(*Departments of Human Anatomy and Orthopædic Surgery, Oxford*)

THE recent improvements in the method of vital staining of cutaneous nerve fibres and their endings with methylene blue have enabled the pattern of innervation in the whole of the skin of the dorsum of a rabbit's ear to be studied. Full details of the method have already been published (Weddell *et al.*, 1940; Weddell, 1941*a*).

It is now clear that each group of hair follicles and each unit area of skin are evenly innervated by fibres which approach from all directions. This is brought about by a scattering, beneath the skin, of bundles of nerve fibres derived from the main nerve trunks which can be observed macroscopically to "enter" the skin. Nerve fibres from such subcutaneous bundles finally form a cutaneous nerve plexus where progressive dichotomization takes place, and each fibre gives rise to multiple endings distributed over an approximately circular area and evenly interlocked with endings derived from neighbouring fibres. This dispersion of nerve fibres beneath the skin is such that each individual hair is innervated by two or more nerve fibres, each of which approaches from a different direction. It has also been estimated that a single medullated nerve fibre in a nerve trunk supplies upwards of 300 hair follicle groups, that is, around 1,500 hairs (Weddell, 1941*a*) (Plate I, figs. 1 and 2).

There is histological evidence of a similar arrangement of cutaneous nerve fibres in human skin (Weddell, 1941*b*), for in Man also nerve fibres can be stained intravitally throughout relatively large areas of skin (Plate II, figs. 1 and 2). In addition it has been found that a cold "spot" in human skin overlies two or more groups of Krause's end-bulbs receiving fibres which approach them from opposite directions, and that in the pad of a human finger (which represents an area of acute tactile sensibility) the Meissner's corpuscles are arranged in groups of two or three and are supplied by fibres which approach them from different directions.

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PLATE I.

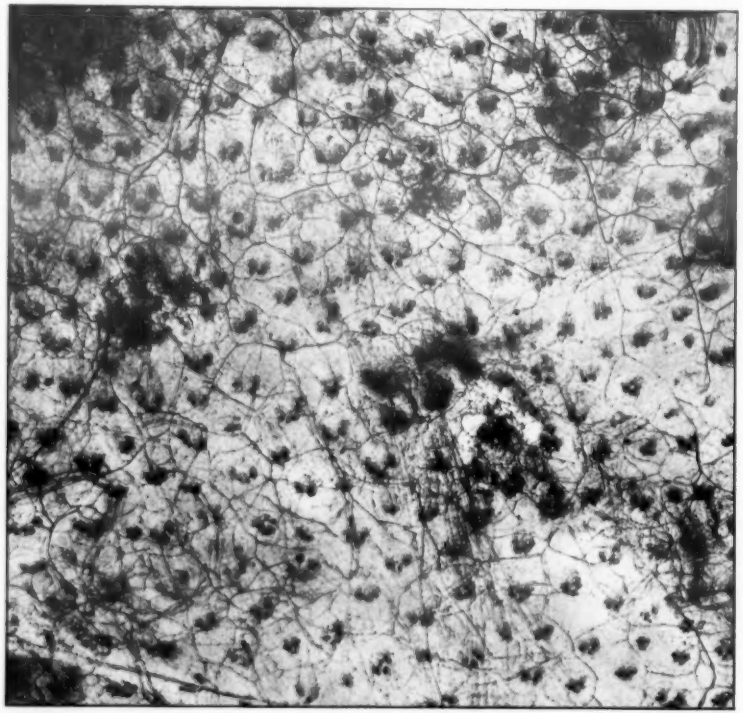

FIG. 1.—A low-power photomicrograph of skin from the ear of a rabbit, showing the scattering of nerve fibres beneath the skin and the formation of cutaneous nerve plexuses. The hair-follicle groups are also stained and are seen to be surrounded by nerve fibres which approach them in all directions from the periphery.

FIG. 2.—A similar preparation under higher magnification, showing how nerve fibres leave the nerve trunks and scatter in all directions beneath the skin. *A* is a blood-vessel: fine beaded nerve fibres can be seen ending on its wall and occasional circular muscle fibres are stained.

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PLATE II

FIG. 1.—Nerve fibres beneath the skin of a human finger pad commencing to scatter in all directions.

FIG. 2.—From the same preparation, showing a similar picture but on a slightly more superficial plane.

There is further evidence of an indirect nature that the pattern of innervation of human skin and that of the rabbit's ear are essentially similar. For instance, recovery of sensibility in a number of cases of peripheral nerve lesions, more particularly those of interruption by inflammatory or crushing processes, is by a general shrinkage of the area of sensory loss from all directions, as opposed to an advancing wave of sensory recovery in the line of the main nerve trunk. Additional evidence is provided by the fact that small incisions through the skin are not followed by extensive areas of surrounding sensory loss. It is also a commonplace observation that in many instances partial interruption of a nerve trunk leads to diminished sensibility in the area of skin supplied rather than to the production of multiple small islands of anæsthesia.

The conception that each single sensory spot is innervated by more than one nerve fibre was crystallized by Head and Rivers (1908) who, on the basis of clinical observations, postulated two different sets of fibres of different phylogenetic significance, and with different rates of regeneration, to account for their dual forms of protopathic and epicritic sensibility. Boring (1916), on the other hand, was led to infer multiple innervation of sensory spots by fibres of a common type to provide an anatomical basis for his own observations on the cutaneous sensory phenomena which follow section of a peripheral nerve and which occur during the process of regeneration, and particularly to explain his ideas of central inhibition.

The histological findings in the ear of the rabbit and in Man, and the clinical findings in Man referred to above, confirm and amplify the postulates made by Boring (1916). The grouping of Meissner's corpuscles to which attention has been drawn is, no doubt, the basis for the great tactile acuity possessed by the fingers, for it clearly provides for spatial summation which allows of the recognition of graded stimuli. It would also seem reasonable to suppose that such an anatomical arrangement may be the basis for tactile localization, for accurate tactile localization implies the recognition of spatial relationships in the skin and it may be argued that such a relationship can only be subserved by at least two impulses transmitted by separate fibres from the cutaneous area stimulated. In addition it has been shown that the sensation of pain is subserved by cutaneous nerve nets which extend over considerable areas—equal in many cases to the distance of "two-point discrimination" for pain in the area in question—which completely interlock with similar nets derived from neighbouring fibres, again providing for multiple innervation of unit areas and at the same time demanding a minimum of dorsal root fibres in covering a large area of skin surface.

In the course of regeneration, nerve fibres will arrive at each separate spot at different times, because they approach it from different directions and the ultimate course to be followed by the individual fibres will necessarily be of different lengths. Thus, in the course of regeneration there will be a phase in which each sensory spot is innervated by a single fibre instead of multiple fibres. During this phase there will be no anatomical basis for spatial summation; therefore reactions to stimuli will tend to conform to an "all or nothing" law, leading to the characteristic explosive type of sensation, and there can be no recognition of gradation and no possibility of accurate localization.

Boring (1916) suggests that if each stimulated sensory spot is projected upon the central nervous system as multiple excitations which depend for their intensity upon their relative strengths, their separation in the region of projection, and upon a limitation of the available amount of central energy, then multiple innervation may be effective either in summation or inhibition of the excitations involved. If this is so, then the recovery of a proportion only of the fibres innervating a sensory spot may give rise to the diffuseness and irradiation of sensation which are experienced. The same thing is seen in so-called "intermediate zones", those areas of diminished sensibility which are found in the zones of overlap between peripheral sensory nerves after section or anæsthetization. In these areas there is an alteration in sensibility which tends to have an irradiating quality, localization is extremely poor and so is two-point discrimination and the recognition of figure patterns traced on the skin. Moreover, histological observations have shown the presence of isolated Meissner's corpuscles and subcutaneous nerve nets in skin from a patient with a partial interruption of the ulnar nerve who displayed an alteration in sensibility similar to that just described. The amount of "wicked pain" (to use Boring's apt expression) varies in different individuals both during regeneration and in "intermediate zones". It is not improbable that some other peripheral factors, perhaps of a chemical nature, are also involved in the production of "wicked pain".

It appears, then, that the anatomical basis underlying skin sensibility consists of specific punctate endings lying at different depths beneath the epidermis (Woollard *et al.*, 1940) and grouped into areas (or interlocked in the case of "pain" nets) which can be defined as sensory "spots". In order that each "spot" shall consist of a number of endings derived from separate nerve fibres, there is a complex scattering of fibres beneath the skin which is expressed histologically as a cutaneous nerve plexus. In the case of an area of skin such as that supplied by the circumflex nerve, the nerve trunk enters the centre of the area of supply and breaks up into numerous bundles which proceed to the periphery of the area and then terminate by the multiple innervation of sensory spots so that the fibres innervating the central area have the farthest distance to travel. Other areas of skin are supplied on a similar principle although in zones such as the digits, multiple innervation is achieved by branches from each digital nerve passing from either side towards the mid-line rather than in a circumferential manner from all sides.

Full details of the anatomical aspect of the findings described in this text have been published in the papers referred to. This work was carried out with the assistance of grants from the Rockefeller Foundation, New York, and the Medical Research Council.

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Meeting at Park Prewett Hospital (American Section)

The Use of Vitallium in Surgery with Special Reference to Cup Arthroplasty

By Wallace H. Cole, M.D.

Chief Surgeon, American Hospital in Britain

Metals of many kinds have been used in bone surgery ever since aseptic technique allowed such surgery to be undertaken; and fixation of the fragments of a compound fracture by nails, screws or wires was not unknown long before anyone dared to make a simple fracture into a compound one. Since the feasibility of operating upon fractures was demonstrated—notably by Lane, of course—innumerable plates, nails and other fixative devices have been designed and used, the majority of these in the earlier days being made out of the then commonly obtainable steels which in later years have been replaced largely by various newer alloys. Many plates became loose, as the screws used to fasten them in place frequently worked out of the bone and no longer served their function. This loosening was usually attributed to infection, and the subsequent necrosis of bone around the metal was thought to be due mainly to this and probably to a lesser extent to pressure. The design of the plates and screws also shared in the blame at times. It is true that some of the older steel plates have remained firmly in position for many years, causing no reaction, but the fact remains that a very high percentage of plates have caused irritative bone changes and have had to be removed later, frequently even before their function had been accomplished. As a result then of clinical experience, sometimes disastrous, many men experimented with new steels and alloys, and the types of screws and plates were repeatedly modified on the principle that infection was not the basic reason for the failures that occurred. In 1924, Zierold published a detailed report on the reaction of bone to various metals in experimental animals and concluded that stellite, an alloy of cobalt, chromium, tungsten and iron, was the least irritating to bone and showed in itself fewer changes in the body than any of the other metals that he worked with. Various so-called stainless steels appeared about this time which were proved to cause little reaction in the body tissues, and, as they combined with this property, strength and ability to be machined, their use rapidly spread, and to-day most bone plates, screws, and pins are made of some form of this ferrous alloy. With the help of the United States Bureau of Standards, a committee of the American College of Surgeons selected vanadium steel as the type best used in manufacturing these appliances, but, in 1936, Jones and Liebmann, in a series of well-controlled experiments, were able to show that a high nickel low chromium steel was more satisfactory. With it the reaction of bone and the corrosive response of the metal seemed to be at a minimum. In this same year Venable and Stuck, while searching for an ideal non-irritating metal, had vitallium suggested to them by a dentist who, with many of his profession, had been using this new alloy for dentures for some years.

This metal was first cast in 1929 as an alloy of chromium, cobalt and molybdenum which is very closely related to the stellite which Zierold used in his experiments. Venable and his associates approached the problem from an entirely new angle and investigated for the first time the electrolytic action of various metals in the body and found that this action was probably the cause of most of the erosion taking place in bone. By their ingenious and carefully planned experiments they showed that vitallium is electrically neutral and is the most "silent" of all the metals and alloys which have been used in the human body. Further experiments and clinical use since then have shown that it is not affected by the body tissues and therefore is not susceptible to corrosion and that it has no effect on the callus nor does it interfere with bone regeneration.

With these results in mind, surgeons, especially in the United States, have been using more and more vitallium in their bone and joint work, always being limited by the fact that the metal cannot be machined or bent, except to a very slight degree, but that all devices made from it must be cast, including the screws. The use is largely limited to bone plates and screws, but various other applications have been found in such things as plates for covering defects in the skull, flanged nails for fractures of the neck of the femur and cups for covering the ends of bones in arthroplasty. Bone grafts are now frequently held in place with vitallium screws, and fractures of many types may be held by screws of various lengths made of the same metal without the use of plates. Subsequent removal of the metal appears unnecessary. Some surgeons have applied vitallium plates to acute compound fractures which are potentially infected, in order to hold the fragments in alignment and give adequate fixation when no other method seemed feasible, the closed plaster being used thereafter. I have had only slight personal experience with this, but I feel that the metal, on account of its complete inactivity in the tissues, may lend itself to this use in some cases, especially in conjunction with chemotherapy. Because of this lack of reaction around the metal many bizarre uses for it also have been devised, although its usefulness is not to be judged by these but by its application to recognized surgical procedures, and I believe it has found a well-deserved place in orthopædic surgery.

Smith-Petersen, who is responsible for this use of vitallium, had for many years been doing arthroplasties of the hip by placing inert glass moulds between the new joint surfaces to prevent re-ankylosis, and he found that the surfaces became covered with a firm, smooth tissue which looked like articular cartilage and under the microscope gave the appearance of hyaline cartilage. Some of the moulds broke, and after experimenting with several other materials he finally devised a mould made from vitallium. Since 1938 cups of this material have been used in many cases by surgeons interested in this work, with good results on the whole. As glass gave way to vitallium, so vitallium is being superseded with some surgeons by moulds made from one of the new plastics, and time alone will show whether this substitution is efficient. The basic principle of the operation does not, of course, rest on the use of vitallium, as such, but has its foundation on the use of an inert, inactive, substance between the freshened bone ends to prevent re-ankylosis. To date, vitallium seems to be the best for this purpose.

I have had occasion to examine two femoral heads and microscopic sections from them after this operation; the first in a case where the patient had been walking for nearly six months and a replacement of a defective cup was necessary; and the second one a month after operation where no weight-bearing and very little motion had taken place on account of the condition of the patient, who died at the end of this time. In neither of these did we find the cartilage mentioned by Smith-Petersen and it is probable that its development depends on longer use of the hip, as one of his two specimens was twenty-one months post-operative and the other twenty-five months. The cup in my six months' case had to be prised from the neck of the femur, all the motion taking place between the cup and the acetabulum. Upon removal of the cup a beautifully shaped, smooth bluish surface was exposed which appeared to be cartilaginous but which was covered by a very thin membrane extending in from the capsule. Similar findings were present on the surface of the acetabulum. A block of bone removed from the centre of the head when examined microscopically, however, showed no cartilage but merely a thin, dense fibrous layer over compact bone. In the second case, the cup was still loose and the stump of the neck was rounded and smooth with irregular islands of what appeared to be cartilage scattered over its surface. Histologically, however, no cartilage was found and the surface was covered with organizing fibrous tissue overlying the bony trabeculæ which showed

atrophy near the surface. These two observations seem to show that extended use of the joint is required before cartilaginous tissue is formed and that probably several years must pass before the final result is obtained. Although it is planned to allow the vitallium cup to remain in place, a second operation for its removal two to three years later might prove to result in a better hip.

As I have already suggested, complications arise in a few cases after cup arthroplasty as might be expected, but these are usually not serious and are frequently due to poor judgment or improper surgical technique. I have seen one hip which dislocated during the first twenty-four hours after operation. In my most interesting case a defective cup split, the only instance reported so far, and the pathology of which I have already described. The patient was a young medical student who was operated upon for a painful hip which followed five years after a traumatic dislocation with immediate reduction. Aseptic necrosis of the head of the femur developed three years later and the head became markedly distorted and flattened with resultant disabling symptoms. Six months after the operation the patient had about three-fourths of the normal range of motion and no pain. Shortly after this his joint started to ache and a few days later he had sudden

FIG. 1.—Radiograph before and after vitallium cup arthroplasty in 54 year old woman with disabling arthritis of right hip.

pain on the slightest motion. Radiographs showed the cup to be split from its rim upward toward the apex for about three-fourths of an inch. The hip was re-operated upon, the condition already described found after excision of a very thick capsule, and a new cup placed over the neck of the femur with an excellent result to date. The thickness of this new capsule led one to believe that it was responsible for some at least of the limitation of motion. As a result of this case, the vitallium moulds are now tested for any defects or weakness before leaving the factory.

The indications for the use of the vitallium cup are those for arthroplasty of the hip by any method, and in addition many cases of arthritis and joint deformity which ordinarily might be arthrodesed or osteotomized can be better treated by this method.

The operation although long is not particularly difficult as a rule, and post-operative pain is surprisingly little in most cases. A detailed description of the operation has already been published, but it must be emphasized that the cup should fit loosely on the neck of the femur, so that motion can take place not only between it and the acetabulum but also beneath it and thus assist in the formation of the new weight-bearing

surface. That it may become tightly attached to the neck later was demonstrated in the case just mentioned which was re-operated upon.

The post-operative treatment is very important and is directed towards obtaining early motion but must in no way interfere with the healing of the wound. The extremity is immediately put up into balanced traction, and even the day following operation a little swinging motion can be attempted. This motion is increased gradually and after two weeks is assisted by passive swinging and abduction and adduction on a board with the heel bound on to a roller skate if possible. A stationary bicycle is also very useful later on, and protected weight-bearing can be started in five to eight weeks if the bone in the neck of the femur was not too atrophied or cystic in character at the time of operation. It is a mistake, I believe, as with all arthroplasties, to expect or force too much motion at the start; this must be allowed to develop by continuous exercise and use. One does not expect to get a full range of action, but a varying degree can be obtained, depending on the patient and the character of the lesion, and this motion is usually remarkably free from pain.

I have performed this operation three times since coming to England, one of the patients aged 61 being poorly chosen and dying within a month of a gangrenous bladder so that the case was a definite failure. The second case was operated upon through the courtesy of Mr. Pridie on March 16 of this year for an osteoarthritis of the right hip (fig. 1). Her chart shows that no morphine was needed after the first night and that on May 31, two and a half months following operation, she had active flexion for 55° from the straight position and 15° more when assisted. Abduction and adduction were reported to be 25° and 40° respectively. It is much too soon to know what the end-result will be. The third patient had what was apparently a congenitally insufficient hip with symptoms of limp and pain since she was 16. At the age of 44 she could no longer walk without great pain. An arthroplasty was performed on May 16, and a somewhat deeper acetabulum was reamed out although the thinness of the ilium prevented the construction of a proper socket. Balanced traction was applied and the patient had no morphia after the first night. She is now standing but the range of motion is still markedly limited. On account of the long duration of the deformity in external rotation—and this is true with many cases—it was impossible at the time of operation to overcome this position of the thigh, and internal rotation is absent.

CONCLUSIONS

(1) Vitallium appears to be a metal which is as inert and "silent" in the body as any alloy yet in use.

(2) When used in any form, plates, screws, moulds, &c., it need not be removed later.

(3) Vitallium cup arthroplasty has a definite place in orthopædic surgery as a reconstructive measure in ankylosing and deforming lesions of the hip-joint.

Sulphathiazole in the Treatment of War Wounds

By James T. Heyl, M.D.

Ten months ago we left the United States at a peak of a clinical enthusiasm for sulphathiazole as chemotherapy for infectious diseases, an enthusiasm which, as American literature indicates, has now moved on to sulphadiazine. This preference for sulphathiazole was based at the time on four claims:

(1) That *in vitro* low concentrations were ten times as potent as sulphanilamide in inhibiting streptococci.

(2) That clinically it was at least equal to sulphanilamide and sulphapyridine in those infections in which they had been found effective.

(3) That it was less disagreeable to the patient and produced fewer toxic symptoms.

(4) That it was effective in mouse protection tests against staphylococci.

It was our privilege to bring over a supply of the drug. We have used it in eighty-three cases of injury, mostly associated with compound fractures, all but eight cases being

at least twenty-four hours old upon transfer here. It has been used locally in the wound as well as by mouth, and it has been used in cases of established infection.

The purpose of this report is to determine whether sulphathiazole has done any patient significant harm and to discuss its pharmacology; the cases are too few to decide whether it has done good.

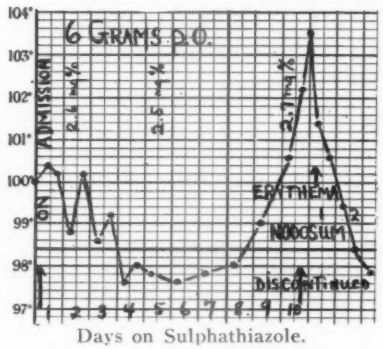
First to consider the harmful effects, for they were relatively clear and few. The doses fell into three groups: four, six and nine g. daily for seven to ten days, being increased as it was observed that harmful effects were few in an effort to secure more definite therapeutic responses. No increase of toxicity was noticed with the higher dosages.

The first chart shows the optimal regime of dosage:

Arbitrary dose regime: 2 g. three-hourly for 3 doses;
1 g. four-hourly 5—14 days.

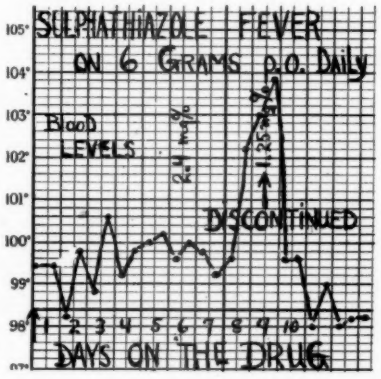
The toxic effects observed are reported on the second chart:

In 83 *cases*: Vomiting 7=8·5%
Skin rash 7=8·5%
Fever 7=8·5%



Days on Sulphathiazole.

Graph 1.



Graph 2.

Vomiting, skin rashes and fever did not occur together in the same cases, as the chart might indicate. In only two cases was it necessary to stop the drug on account of severity of the vomiting.

The skin rashes were striking, and unique in chemotherapy. Four were red, nodular, non-itching, slightly tender lesions on the shins and ulnar regions looking just like erythema nodosum. They are described in Boston and Philadelphia literature, and there has been one other case in this hospital. The rash came on the sixth to tenth day at normal blood levels for the dosage and disappeared within two days of stopping the drug. The other three were nondescript papular eruptions on the face and neck, and a trunk erythema.

The most picturesque of the sulphathiazole fevers is copied on these temperature charts. The points of interest in the graphs are the steady rise, without daily return to normal, and the constant blood-level of 2·4 mg.%. Because we expected more renal and blood disturbances, urine and blood examinations were carried out on almost all the patients, including every one with toxic symptoms. Microscopic hæmaturia was rare and never exceeded two to three red cells per high power field. The one gross hæmaturia was in a patient with a ruptured *Proteus*-infected bladder and preceded sulphathiazole.

There was no harmful effect on the hæmatopoietic system at all, as judged by red or white cell counts.

The absence of renal complications we attribute to our insistence upon a fluid intake of 100 oz. daily. It remains a major concern, for acid urines coming to the laboratory show, after standing, as much as ½ in. crystalline sulphathiazole sediment in a jam jar. Fig. 3: Urine concentrations up to 450 mg.% increased our concern because sulphathiazole is soluble in distilled water only to about 20 mg. Alkalinity of the urine increases this solubility, reducing the sediment.

Therefore it is fair to say that sulphathiazole has done no detectable harm, though its excretion as a hypersaturated urine is a real hazard. But it is only fitting to comment that most patients are very grateful to be off the drug.

At Dr. Cole's suggestion 30 cases admitted for knee operations were used to establish the diffusion of the drug into joint fluids. Two of these were septic and found similar to the rest. The patients were given 10 g. of sulphathiazole in 18 pre-operative hours, and synchronous blood and joint level determinations were made. Since novocain gives

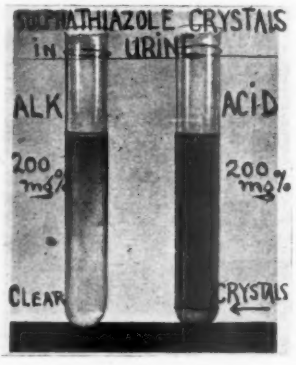


FIG. 3.

the same colour reaction as sulphathiazole in the Marshall-Bratton technique, inhalation anæsthesia was used. The extremes of blood levels were from 2·8 to 12 mg.%, averaging 6·1 mg.%. Corresponding knee-joint levels were about the same: 20 averaged 1·2 mg.% higher, 7 were 1·1 mg.% lower. The percentages of the total of the free, active form of the drug in the blood averaged 86%. That of the joint fluid was slightly less, 80%, perhaps indicating a tendency of the acetylated, inactive form to accumulate in the joint. The significant conclusion from the series was that the sulphathiazole level of knee-joint fluid is as effectively high as the blood level.

Sulphathiazole was given by mouth for two distinct purposes:

(1) To prevent infection, because the circumstances in which operations were performed were not ideal.

(2) As a therapeutic agent: To eliminate or limit bacterial infection.

To gain a prophylactic effect, the obvious ideal is to produce a blood level of at least 2 mg.% at the time of operation. This implies a dose at least four hours pre-operatively and we have said, five days post-operatively. To evaluate its effect as a prophylactic, a control series would be necessary. As this is not available we are limited to crude gauges of effectiveness, for example:

(*a*) Of 213 patients subjected to clean surgery, in only one, this one receiving sulphathiazole, has the surgical result been marred by infection; staphylococci were grown on culture.

(*b*) Administration of sulphathiazole does not prevent suppuration around pins in a significant percentage of cases; within ten days of removal of the pin, the condition subsides.

With large wounds, it is difficult to assess the therapeutic effectiveness of sulphathiazole by oral administration. It was particularly so in our series because infection of the wounds was usually well established, and they were enclosed in plaster.

The distribution of blood levels in 25 patients on 1 g. four-hourly with forced fluids for five to fourteen days, was between 2 and 6 mg.%, mostly between 2 and 4.

In a smaller series receiving 1½ g. four-hourly, the grouping was between 3 and 7 mg.%.

Although there was no corresponding gradation of effectiveness, these give an idea of the blood levels at which the observations were made.

Two criteria were used: the temperature chart, and modification of the bacterial flora.

There were 9 patients with a temperature of 101° for from five days to three weeks; this was reduced to 99° or less within forty-eight hours on sulphathiazole. All these patients but one had cultures of either hæmolytic streptococci or pneumococci, but since 5 of the patients were suffering from pneumonia we are left with only 4 with wounds whose fever was high for long enough to show a striking fall in response to sulphathiazole. Of these 4, the 3 with cultures before treatment showed hæmolytic streptococci along with a mixed flora.

By the same criterion of fever, there were two sulphathiazole failures. It is of interest that, in contrast with the behaviour in successful cases, their infection extended and pocketed. The wounds in both these cases were found to contain streptococci, which by a technique shown us by Dr. Colebrook were resistant *in vitro* to 1:25,000 (4 mg.%) concentrations of sulphathiazole. One was a hæmolytic, the other a fæcal streptococcus.

As to general bacteriology, certain miscellaneous points emerged. No wound was freed of staphylococci, *B. pyocyaneus*, coliform bacilli, or diphtheroids in which the change could not have been attributed to time and epithelization. Of 9 patients from whom *Cl. welchii* were grown, 2 underwent amputation, 2 others developed subcutaneous gas and in the other 5 they were just chance findings. The *Cl. welchii* disappeared from all of these following topical and oral sulphathiazole, even under plaster.

It is obvious that in the majority of cases with little or no fever, and a mixed bacteriology, the effectiveness is a matter of impression about which even the observer cannot be certain. From the effect on the course of the fever the impression is gained that sulphathiazole benefits wounds containing sensitive hæmolytic streptococci, but conclusive, bacteriological proof is not available.

The use of sulphathiazole applied locally as an antiseptic agent has been tempting because of its potency *in vitro* and the theoretical advantage of greater local concentrations by this method. It is questionable whether, insoluble as it is, its deleterious action as a foreign body does not outweigh its advantage as an antiseptic. For there is no doubt that with our technique of application it persists as lumpy masses; it is not uncommon to find it in vaseline packs after two to three weeks, and in bony recesses we have observed it after six weeks.

Data on the amount absorbed is provided by six patients who received no sulphathiazole by mouth. In each a weighed amount of 1-4 g. of sterilized sulphathiazole powder was tapped from a test tube into the wound and spread to a thin coating with an instrument. There were no blood levels over 1·5 mg.%, and this whether it was put in an old osteomyelitis cavity or sewn tightly in an amputation stump. Traces appeared in four hours and persisted as long as fourteen days. The inaccuracies of determination under 1 mg.% make detailed conclusions from the data useless.

There were only four fresh cases in which sulphathiazole was enclosed in sutured wounds. Two were cases of amputation above chronic hæmolytic streptococcal infection.

All four cases showed healing by primary intention, with no evidence of foreign body irritation.

Opinion is divided as to whether there has been a deleterious effect on epithelization and on the formation of granulation tissue. At any rate there is no obvious constant beneficial or deleterious effect.

The small number of cases and the uncertainty of the cultural technique does not warrant any conclusion regarding topical sulphathiazole.

SUMMARY

In the use of sulphathiazole in infected wounds:

(1) There are relatively few, and these only minor, toxic reactions with large doses when adequate fluids are given.

(2) The drug reaches knee-joint fluids in about the same concentrations as the blood.

(3) Judged by the reduction of high fevers in streptococcal infections, sulphathiazole has been definitely beneficial in four cases.

(4) There are, however, hæmolytic streptococci resistant to sulphathiazole.

(5) Its value prophylactically and topically is still in the observation stage.

Mechanical Fixation of Fractures

By Charles H. Bradford, M.D.

There are three accepted methods of treating routine fracture cases: Closed reduction, open reduction, and traction. Each method has special applications for special types of fractures, but all three are in general use.

There is a fourth method of treatment derived from the principles of mechanical fixation; that is, by fixing a fracture at both ends, by means of pins or screws, and then utilizing the fixation units to accomplish the reduction and the immobilization of the fracture. These principles involve certain departures from routine methods, and their success or failure will depend on three critical points which are still very much in debate, namely infection, technical efficiency and practical results. (1) Can pins or screws be used for skeletal fixation without undue risk of infection? (2) Will mechanical apparatus be able to accomplish reduction and immobilization effectively? (3) From a practical standpoint, will the use of apparatus introduce factors which may hinder or interfere with the recuperative process?

I shall begin by emphasizing the dangers and defects which accompany the use of mechanical apparatus. Probably surgeons will agree that the most obvious danger is from contamination of the pins. This can occur through several different channels. Unless strict asepsis is observed at the time of insertion, the pins may carry bacteria directly into the substance of the bone. Here is a danger which cannot be over-emphasized, no matter how elementary it may seem. Only the surgeon who realizes it fully and dreads its consequences can be relied upon to avoid it. A second route of contamination will occur through the sinus tract which forms around the pins as long as they remain in place, draining a minute or copious serous discharge caused by the foreign body reaction and by the irritation of soft parts. This sinus does not prove as dangerous as might be expected. One reason may be that it always affords unobstructed drainage outward, provided the dressings are properly applied. Furthermore a patient of normal vitality probably possesses enough tissue resistance to counteract the slight bacterial invasion which occurs at the entrance wound. Possibly a debilitated patient with lowered resistance, or, a diabetic, would offer a more serious risk from this standpoint. Still another factor limiting the danger from the sinus lies in the fixation of the pins themselves which are so firmly held that no motion whatever, either outward or inward, is permitted. In this respect, the apparatus of mechanical fixation has proved safer than the more common practice of Steinmann

pin insertion above and below the fracture, where adequate precautions may not be taken against pins sliding through the bone. A third avenue for infection to enter the pin wound is through the blood-stream, as is the case in the common form of hæmatogenous osteomyelitis. The bone area that has been damaged by pin fixation would offer a focus of minimum resistance in which bacteria might incubate. With this in mind, it has seemed wise to administer chemotherapy whenever a septic flare-up appears on the patient's temperature chart. Here again, however, the danger seems to be greater in theory than in practice, and the defensive reactions of the tissues seem to be ample to meet the trauma of pins. Evidence of this lies in the success we have found from using pins on infected, compound fractures, the results of which will be discussed later. With pin treatment we should consider the wound as being potentially infected. Unless we treat it from that standpoint the potentiality may become a reality.

From the technical standpoint we are faced with the problem of adapting a machine to the complicated manœuvres of fracture treatment, and here we encounter a very real difficulty. No one should suppose that the machine offers an easier method of handling fractures. In fact, it may offer what will at first seem like a harder method, because the machine has substituted complex screw-traction and lever-arms and rotating bars for the familiar manipulation of closed reductions. Consequently the surgeon must teach himself all over again to do in a mechanical way what he has been used to doing directly with his hands—just as a boy at school who has learned handwriting with a pen must learn all over again if he wishes to write mechanically with a typewriter. If the surgeon will school himself in this way, he will find that the machine can reproduce every manœuvre he desires; and can, in fact, accomplish many adjustments that could not be attained by simple means. Thus, it emerges, that the technical difficulties, which are so very real that they deserve this emphasis, do not reside so much in the machine itself as in the surgeon who uses the machine.

There is still a third aspect of mechanical fixation which raises legitimate objections or doubts. Any form of treatment that tends to fix fracture ends in a position of distraction, cannot fail to delay and perhaps prevent union. Unless we recognize this fact, we are flying in the face of trouble; and yet with pin fixation we stand in danger of making this very error, since the pins allow no backward slipping and their position has been locked in place. For this reason, there is nothing worse, to my mind, than to call this machine a "distraction apparatus". Here, our critics may become our teachers; and from their observations we must learn to convert it into an impaction apparatus. Following the reduction of the fracture, we should in every instance, release the traction screw and force the fracture ends together, even if this manœuvre forces the fragments into slight over-riding. By doing this, we produce a controlled impaction which is of the utmost importance. Anderson insists on X-ray examination at the end of two to three weeks, to see if any absorption has occurred at the fracture site. If it has, he locks the fracture in the apparatus and again impacts enough to force the ends into complete apposition. If this procedure is carried out, mechanical fixation becomes a treatment of persistent, controlled impaction, which offers an advantage over any other method available, except for cases suitable for walking casts. Nevertheless, we must realize the ever-present danger of distraction if we are to counteract it. If it is ignored, it will constitute one of the most serious defects in the treatment.

Although other, minor difficulties of a technical nature will appear, those that I have mentioned are the major ones affecting the principle of mechanical fixation. From this brief review it should be evident that they are serious enough to require careful attention; but that once they have been recognized and studied they may be mastered. Space does not permit any further details of the different types of apparatus which have been devised for this purpose; nor is there time to mention the names of various outstanding surgeons who have contributed to it. Forty years ago, the Belgian surgeon Lambotte anticipated all that we are doing to-day, and achieved remarkably good results. It cannot be said that Roger Anderson imitated him, for Anderson has revolutionized the apparatus and developed wholly new principles for its application.

The advantages of this form of treatment require less discussion than the difficulties; for most surgeons would agree that, if its defects can be overcome, its merits will be sufficiently apparent. Briefly stated, these can be summarized under four headings. First, it gives us a more powerful and a more accurate means of reducing difficult fractures. Then again, having completed the reduction, it provides an almost vice-like form of

fixation. Furthermore, such fixation, properly applied, avoids the delay to union produced by distraction. While this effect cannot claim to hasten or stimulate the healing of a fracture, it has the negative, but very real value of preventing unnecessary delay. Lastly, the treatment allows free ambulation from a very early period.

Operating as a base hospital, we find that the fractures which drift back for our care are the more difficult ones, and these generally reach us at a comparatively late stage of their progress. This must necessarily prove to be the case since "blitzed" hospitals can afford neither the time nor the facilities for specialized fracture treatment. The result

Ambulatory treatment of fractured femur with Roger Anderson pins and bar—ten days after pin fixation.

is that many of our fractures have passed the stage where simple attempts at closed reduction would be effective. Mechanical apparatus has proved of great value in such cases.

Another result of war conditions is the frequency of dirty compound wounds. A large number of these fractures require some form of open reduction, but that is prevented by infection. The Orr-Trueta closed plaster treatment offers a solution to the problem of infection, though it often fails to solve the fracture problem so satisfactorily. Mechanical

fixation has provided a means of forced correction that can be used in the presence of infection and may be combined with closed plaster treatment. This also gives us a form of external skeletal fixation, when used with a bar, which will be of unusual value in cases where the wound needs to be skin-grafted.

Finally, the ambulatory form of treatment is very valuable in time of war, as evident from the various campaigns fought on far distant fronts. The American Army has recognized this benefit of mechanical fixation and has, I understand, equipped a number of base hospitals with the apparatus. This was not done without trial of the method by Colonel Sloat of the Walter Reed Hospital, where a series of cases were treated and their results approved. In addition to the Services, it would seem most desirable to make all the air-raid casualties as ambulant as possible. The patients then become more freely transportable from one hospital to another; and in case their hospital is bombed, they have a far better chance of escape.

It was largely the appreciation of such war conditions which influenced Professor Wilson to bring this equipment with us. Not only did he authorize the use of the equipment, but he took the responsibility for applying it, as Anderson also had done, to grossly septic cases which at first seemed too hazardous to attempt. The remarkable results more than vindicated his bold judgment. The name of Mr. W. R. Ferguson should also be mentioned, as he brought with him an equivalent apparatus contributed through the generosity of its inventor, Mr. Haynes. He had gained his experience with this apparatus at the Johns Hopkins Hospital in Baltimore, and was able to teach us its management. Third in the trio of our benefactors in this field was Mr. F. E. Waknitz, who designed and manufactured by hand a miniature device which we have since called the "Waknitz apparatus". It incorporated the principles of the Anderson pins. He used this with great skill on a metacarpal fracture which was referred to him through the courtesy of Colonel Cone. Also, through the courtesy of Sir Harold Gillies, he used it on a fractured jaw case which he and Mr. Converse treated most successfully. This is the first time such treatment has ever been applied. Its success was such that it has awakened a great deal of interest, and has been copied or modified by a number of surgeons. It is likely to develop into a very useful contribution.

In a war hospital we are unable to obtain follow-up studies; and it is much too early to pretend to end-results. We have thus far treated 41 cases, many of whom are still in our wards or convalescent.

TABLE I.—DISTRIBUTION OF FRACTURES TREATED BY MECHANICAL FIXATION.

Femur	22
Tibia and fibula	11
Metacarpals	3
Humerus	2
Radius and ulna	2
Jaw	1
Total	41

There is considerable interest in the skeletal distribution in Table I because of the preponderance of lower extremity fractures. We feel very strongly that this method of treatment should not be applied to fractures which can be adequately treated by conservative methods. As a general rule, our real problems have occurred in the lower limb. Our attitude is not based simply on a desire for ambulation under war conditions. We hope to avoid the long, debilitating period of bed immobilization and to fix the fracture ends in immovable apposition. The patient gets a better reduction, surer fixation, and improved muscle tone. This should stimulate the circulation and promote callus. It is not felt that we gain any earlier knee motion by this method, as a patient can move his joint only a moderate amount with pins in place. However, we have not found any greater damage to the knee than in routine traction treatment, and, when not complicated by special factors, the motion is regained in a normal length of time.

TABLE II.—INTERVAL BEFORE MECHANICAL FIXATION.

Immediate (up to 2 days)	3 cases
Early (up to 2 weeks)	18 cases
Delayed (up to 11 weeks)	12 cases
Late (3 months to 6 months)	8 cases
Total	41

Table II gives roughly the age of the fractures at the time we have been able to treat them, and emphasizes the difficulties under which we have been working. It sometimes seems unfair to submit a new method of treatment to such a severe initiation. Even so, the fractures, up to two weeks old, have generally yielded excellent results; and we have often been surprised at the success which can be obtained in still older fractures. For example, a nine-weeks' old tibia and fibula fracture, with complete displacement and over-riding, was sent to us a few months ago. Five attempts at reduction had been made in another hospital, and, though these succeeded, the fracture had slipped each time. At the last attempt an open reduction had been carried out without fixation. This too had been followed by slipping, and the operation wound had become superficially infected. By means of the apparatus, however, Mr. Hall of our staff was able to obtain an almost anatomical reduction, which was maintained until solid callus formed within nine weeks. This is by no means a usual experience, but it illustrates the possibilities. Success in these cases will depend a great deal on the operator's familiarity with the mechanical control of the apparatus; and even more upon his patience and faith in its capacities.

Our very late cases were frank attempts to see if this method is applicable to older, delayed-unions of fractures. It is still too early, and the cases are altogether too few to give any report on them as yet, though some results are encouraging. If we were dealing with a complete non-union there might be no justification for this trial.

TABLE III.—INCIDENCE OF INFECTION.

Original condition of fracture		Bone infection resulting from pins
Simple fracture: Without infection	27	0
Compound fracture: Infection a minor factor	5	0
Compound fracture: Infection a major factor	9	1
Total	41	

Table III presents a part of the picture of the incidence of infection; but I should like to make it clear that it is only a part. We have found, and Anderson has already shown, that the skin in an ambulatory patient will inevitably pull a slight amount against the shaft of a pin. The commonest site of this irritation will occur in the upper pin of the femoral unit. The result will be a foreign body reaction, with the discharge of serum. In many such cases there will be contamination enough to cause superficial infection; but this discharge is really harmless and clears up as soon as the pins are removed. The more interesting cases have been those where pins have been used in close approximation to infected compound wounds. The most outstanding case of this sort was a boy treated by Professor Wilson and Mr. Dial. He had a huge compound wound of the thigh; the femur was splintered for several inches, and it was saturated with infection which grew cultures of *Cl. welchii,* staphylococcus, and streptococcus. The injury was a week old when we began treatment. Pins were inserted and combined with a bar for immobilization as well as closed plaster to support the wound. The pins remained in the bone approximately six months. During this time, the plaster was changed three times, but the pins and bar prevented any motion to the fracture itself. At the end of six months, callus had formed solidly, and the wound was two-thirds epithelized. The pins were removed, but the patient was given the support of plaster for another month. He is now clear of all support and is beginning to develop knee motion. He has half an inch of shortening and a knee which allows only 10° of motion. While this case is very striking, our other grossly infected cases have all done as well with the exception of a single one, which still shows a slight discharge from the pin track. Though it is a low-grade infection and the discharge is only slight, I think it must be considered an actual bone infection. On the whole, however, I believe the total results of this series are encouraging. The final answer as to the true risk of infection can only come from large numbers of cases followed in several clinics. Within a year or two we are likely to have such data.

SUMMARY

(1) Here is a new method of treatment on trial. It is not presented as a universal treatment, but as one which offers special advantages for special types of cases.

(2) Its particular advantages are that it can be used in the presence of infection; that

it provides powerful and precise means of reduction and firm fixation, and that it allows free ambulation.

(3) Its dangers and difficulties must be carefully studied by surgeons who undertake to use it, since their own experience and lack of understanding will contribute largely to the failures they may encounter.

(4) The danger of infection is as yet undetermined; but indications suggest that this factor will not be a serious bar to its use when careful aseptic technique and vigilant follow-up care are observed.

Orthopædic Aspects of Plastic Surgery
The Early Replacement of Skin Losses in War Injuries of the Extremities

By John Marquis Converse, M.D.

Injuries of the extremities occurring in modern warfare often produce wounds with extensive skin losses creating special problems.

These wounds may show skin destruction tending to encircle the limb. The spontaneous healing of such a wound may result in constriction and consequent circulatory disturbances in the extremity.

Contractures resulting from a wound near a joint may limit its function.

In compound fractures, one or many wounds may be found, either in direct relation to the fracture site or only in the proximity of the fracture. When the wound presents a considerable loss of superficial tissue healing may be incomplete and of poor quality, giving an inadequate covering to the fractured bone. Infection may delay healing and consolidation of the fracture. Under plaster such a wound, a natural culture medium, may discharge an abundant and fœtid purulent exudate, of rich and varied bacterial flora. Great delay in the performance of important secondary bone, nerve or tendon surgery may be due to the presence of an unhealed wound under plaster.

When bone is exposed through the loss of the superficial covering and periosteum, it becomes devitalized, sequestrated, and is open to infection and osteomyelitis. Tendon left uncovered is destined to slough.

To restore normal function to the extremity, extensive secondary plastic reconstructive operations are often necessary, further delaying the patient's return to active work. Many of these late complications could be avoided by the early replacement of the skin loss.

Pathology of the unhealed wound.—The importance of early wound epithelization is emphasized by the study of the changes that occur in a wound failing to heal rapidly.

In normal wound healing a double regenerative process occurs, that of connective tissue, and that of epithelial tissue. Healing is not achieved until the new connective tissue, known clinically as granulation tissue, is covered by a continuous layer of new epithelium. Certain pathological changes are noted in wounds presenting a failure or a delay to become covered by regenerated epithelium.

Sections made of young granulation tissue show numerous newly-formed blood-vessels and fibroblasts. The latter are aligned parallel to the blood-vessels.

In older granulation tissue, often in wounds three to four weeks old, towards the base of the layer of granulation tissue, the fibroblasts assume a more horizontal direction, thus tending to be perpendicular to the blood-vessels. At the same time between the fibroblasts appear connective tissue fibres and collagen (fig. 1).

As the unhealed wound grows older this deep layer of fibrous tissue tends to increase at the expense of the superficial layer of granulations. Large numbers of capillaries are obliterated thus depriving the superficial layer of granulation tissue of some of its blood

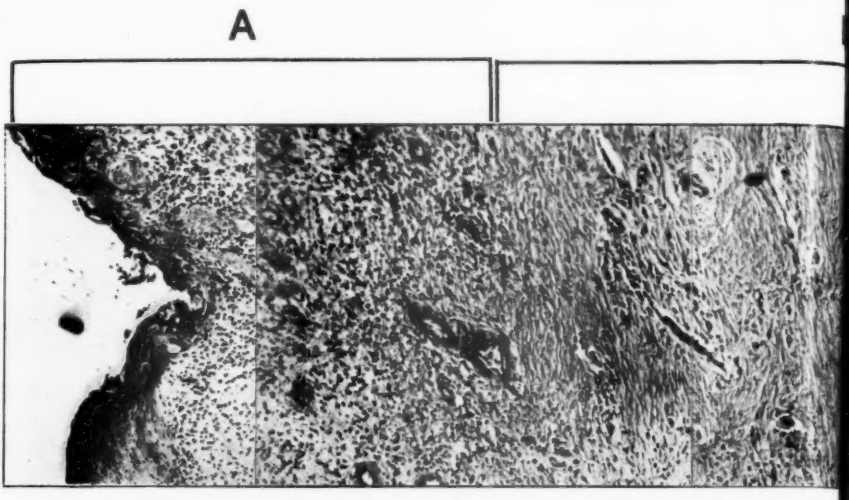


FIG. 1.—Section showing fibrotic ch
A.—Granulation tissue showing inflammatory changes.
B.—Organized granulation t show nuclei which have as pendicular to the blood-vessels

supply. The granulations tend clinically to appear cyanotic and œdematous from venous congestion, first evidence of impaired circulation, improved by pressure over the wound.

The deep fibrous layer slowly invades the superficial granulation tissue, the surface of which tends to become necrotic through defective circulation and secondary infection. Finally the whole wound tends to become a mass of fibrous tissue.

It can thus be seen that the pathological picture of an unhealed wound is one of a gradually diminishing blood supply, and of a progressive increase of fibrous tissue. This produces an increasingly unfavourable base for the spread of epithelium and predisposes the wound to secondary infection.

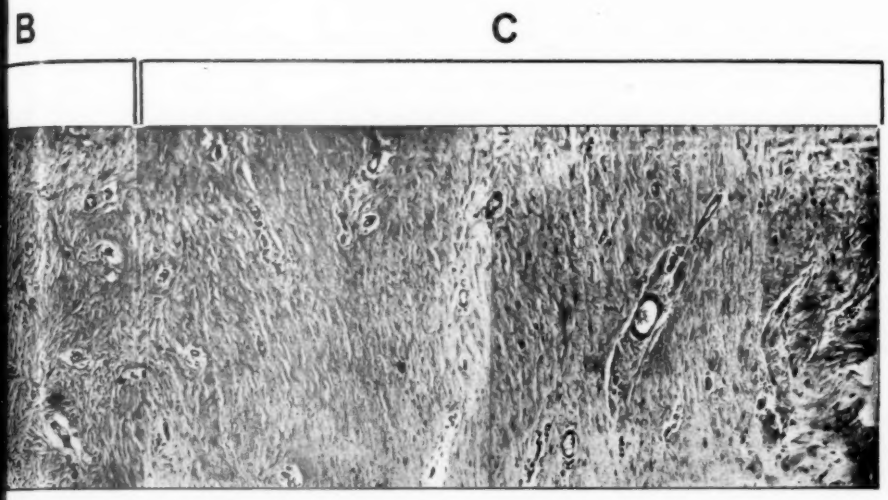
Role of infection.—The presence of pus appears to be detrimental to epithelial growth in general. Furthermore certain organisms seem to have a specific inhibiting action on new epithelium. This is particularly true of various types of streptococci. Colebrook and Francis[1] have reported the remarkable growth of epithelium following the disappearance of the streptococcus from superficial wounds after local applications of sulphanilamide powder.

The œdema which accompanies acute inflammation may prevent a very important phenomenon in wound healing, namely contraction.

Importance of wound contraction.—Starting early in the process of healing, continuing during and even after epithelization, contraction of the wound takes place.

Primary contraction follows a "silent" or "lag" period during which, through phagocytosis, the elaboration of enzymes and exudation of lymph, the wound rids itself of devitalized tissues and foreign bodies. Its occurrence is greatly hastened by excision of the destroyed tissues. It is probably due to the pull of elastic fibres of the connective tissue in and around the wound. It is an effort to make the wound smaller, and close it off from the surrounding tissue.

[1] COLEBROOK and FRANCIS, Elimination of Streptococci from Superficial Wounds by Sulphanilamide Powder, *Lancet*, 1941 (i), 271.



ound unhealed for four months.

fibroblasts C.—Fibrous scar tissue with collagen formation and obliteration of blood-
osition per- vessels.

Secondary contraction takes place later in the process of healing. Fibrous tissue increases in the wound. This late contraction tends to bring the epithelial edges of the wound closer together and it is the cause of constrictions, contractures and deformities of the extremities. The longer the wound remains unepithelized the more marked these deformities will become.

Primary contraction constitutes one of the most important elements of wound healing. It greatly diminishes the size of the wound that is to heal. In deep wounds contraction pulls the surrounding tissue and muscles into the defect to fill it.

Primary wound contraction is such an important element of wound healing that it is possible, to a certain extent, to predict the rapidity and the quality of the wound repair according to whether the wound is situated in a position favourable, or one unfavourable, for wound contraction. Contraction occurs best where muscle tissue is abundant, so that it can be stated that, in a general way, contraction and thus wound healing is directly proportionate to the amount of muscular tissue around the wound. To cite the lower extremity as an example, wounds of the thigh generally heal well, wounds of the anterior tibial region heal poorly.

The size of the wound has a bearing on the evolution of healing. Epithelial regeneration, through a process of cellular enlargement, multiplication and migration, proceeds at a certain rate. If the loss of tissue is large and if it is in an unfavourable situation for contraction, epithelization of the wound will take a certain length of time during which the fibrous changes previously described may occur. One frequently sees large wounds over the tibia, healed but covered by epithelium resting on poorly vascularized fibrous tissue. This poor covering for the bone, destined to break down, appears to bear some of the responsibility for the chronicity of osteomyelitis of the tibia.

The "vicious circle" of the unhealed wound.—Where the skin loss is extensive, when wound contraction is poor, fibrous tissue is formed, the circulation of the wound is impaired, infection occurs and impairs epithelial growth, more fibrous tissue is deposited; this cycle can repeat itself indefinitely; the result is an unhealed wound.

From these considerations one is led to conclude that the rapid covering of the wound by epithelium is desirable; if spontaneous epithelial regeneration appears difficult it is preferable to resort to the artificial provision of epithelium through skin grafting.

INDICATIONS FOR SKIN GRAFTING

A skin grafting operation should be considered:

(1) *When the skin loss is such that it appears probable that impairment of function of the extremity will result.*—This applies particularly to wounds about the joint surfaces, and to wounds which tend to be circular and liable to cause constrictions and circulatory difficulties.

(2) *When spontaneous healing of the wound appears improbable.*—In the aged, the debilitated; when the wound is in an unfavourable anatomical situation overlying bone.

(3) *When rapid healing is desirable.*—Skin grafting makes possible at an earlier date secondary operations such as nerve suture or grafting, secondary tendon suture, secondary bone surgery. In such cases epithelial healing may be achieved in ten days when spontaneous epithelization may be prolonged over months.

Skin grafting of open granulating wounds.—At the suggestion of Colonel Leonard Colebrook and of Sir Harold Gillies a study was made of one hundred and ten skin grafting operations performed between October 1940 and June 1941 at Rooksdown House, Park Prewett Hospital, upon infected granulating wounds. Records were kept of the date and cause of the injury, the date of the skin grafting operation and the bacteriology of the wound before and after operation; the percentage of success of the skin graft was noted, 100% representing a complete "take". The operative procedure and post-operative follow-up were noted.

Besides technical details of fixation of the graft, adequate pressure, &c., two main factors were found to influence the success of the skin grafting, wound infection and wound fibrosis.

(1) *Wound infection.*—Infection creates suppuration. Purulent exudate will lift the graft away from the wound, thus preventing its adherence and "take". Failure due to suppuration may occur in the presence of any pathogenic organisms.

Certain organisms appear to have a specific action upon the take of the graft.

In presence of an acute hæmolytic streptococcal infection (untreated by specific chemotherapy) skin grafting is generally unsuccessful. Amid signs of acute inflammation the wound is filled with the serosanguineous pus which displaces the graft from its bed. A dissolution of the layer of fibrin which causes adherence of the graft appears to take place, probably due, as suggested by Colebrook, to a fibrolysis of the streptococcus. A late ulcerative action frequently observed in grafts that have appeared successful, is found to be due to the hæmolytic streptococcus. If uncontrolled it may destroy the whole graft.

The advent of chemotherapy has allowed a great control over the hæmolytic streptococcus. With the collaboration of Colonel Colebrook and of Major Francis it has been possible to obtain streptococcus-free wounds usually within a few days after initiation of treatment. By freeing the wound of purulent exudate, by means of dressings, baths and methods of mechanical irrigation, the anti-bacterial action of sulphanilamide powder applied locally can take place.

In this manner it has been possible to perform skin grafting upon wounds presenting cultures free of hæmolytic streptococci.

A sulphanilamide-resistant streptococcus persisted in nine patients. Skin grafting performed in the presence of this organism was generally unsuccessful.

Local sulphanilamide powder was used in most cases over the wound before application of the graft. The drug was insufflated as a thin layer of powder with Pearce's insufflator or massaged into the wound (Mowlem).

No evidence could be found that the presence of sulphanilamide beneath the graft interfered in any way with the take of the graft.

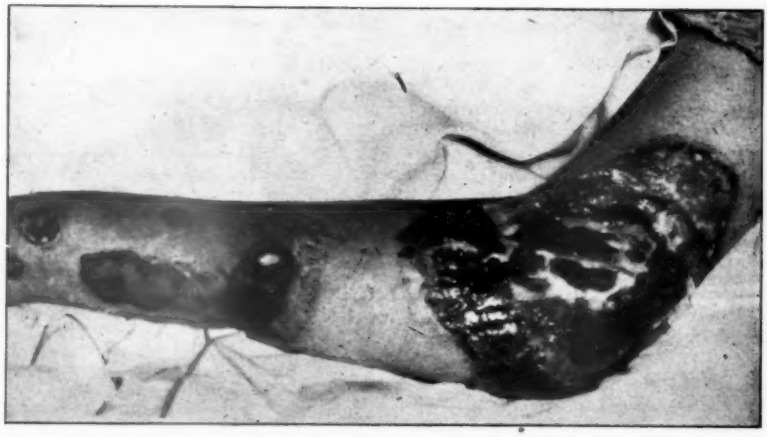


FIG. 2.—Appearance of wound of elbow following crushing under debris of a bombed house. Note gangrenous slough.

FIG. 3.—Ten days after secondary excision and skin grafting in presence of streptococcus (type A) and *B. pyocyaneus*. Sulphanilamide powder applied to the wound before grafting. Oral sulphanilamide.

The clinical value of this local chemotherapy at the time of operation is demonstrated by the fact that all complete failures due to a streptococcal infection were found to have been without this added protection or to have presented a sulphanilamide-resistant streptococcus. In five wounds skin grafting was carried out successfully in the presence of hæmolytic streptococci (type A) with the aid of local and oral chemotherapy. If furthermore one considers that 72% of these granulating wounds were found to have been infected by hæmolytic streptococci the importance of chemotherapy is evident. Oral sulphanilamide was administered in doses of from 3 g. to 6 g. daily in the adult over a period of from three to seven days in those patients whose wounds were recently freed of streptococci.

The *B. pyocyaneus* causes a failure in most cases where skin grafting is attempted in its presence. Through probably a proteolytic action of the organism the graft becomes very thick, greasy in appearance and finally is removed as a slough. Practical failures were observed in the five cases grafted in presence of *B. pyocyaneus*, without wound excision. In five cases grafting was performed after excision of the wound; of these, in two cases

FIG. 4.—Appearance of healed wound three weeks later.

the graft was successful and there was no reappearance of the organism; in three cases grafting was nearly completely successful, a recurrence of the *B. pyocyaneus* being noted but the wound healing rapidly by second intention. It appears to be a distinct advantage in wounds containing *B. pyocyaneus* to perform excision before skin grafting, as this organism does not appear to thrive in freshly exposed tissues.

The influence of *B. proteus* upon skin grafting was not observed.

The staphylococcus seems to influence the take of the skin graft only in proportion to the amount of exudate produced in the wound. Most cases of complete take of grafts were noted to have presented staphylococci and diphtheroids at the time of operation. Wound healing and consequently successful skin grafting does not depend totally upon the bacterial status of the wound. A wound may be sterile but present no evidence of healing.

(2) *Wound fibrosis.*—The production of fibrous tissue in the deep layer of the granulation tissue of the wound, diminishing the local blood supply, tends to create a poor base for a skin graft. It would seem preferable therefore, particularly in older wounds, to excise the wound whenever this is possible, to obtain a vascular base for the graft.

Statistics showed that when excision of the wound had been performed the percentage of graft-take was 88%. When wound excision was not done the percentage of graft-take was 52% (fig. 5).

After wound excision 52% of the cases presented a primary graft-take of 100%. Without wound excision a primary graft-take was observed in 12% of the cases.

Secondary excision.—This consists in excision of the whole wound until tissues of normal appearance are exposed. Upon this vascular muscle or fascia the graft is applied. The great objection to this procedure in an infected wound is the possibility of a flare up of a quiescent infection, particularly streptococcal. It is felt that local chemotherapy as an adjunct to secondary excision prevents such an occurrence. Complete secondary excision, however, is not always feasible, particularly for anatomical reasons, the proximity of bone, of a joint capsule, of important vessels or nerves. In such cases the removal of the infected granulations down to the fibrous base, by eliminating the pus-producing

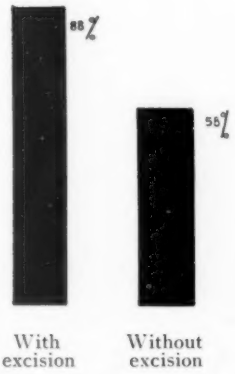


FIG. 5.—Percentage of skin-graft "take", illustrating importance of wound excision before skin grafting.

tissue will give a greater chance for the skin graft to take than if the graft is applied to the untouched granulations.

Observations on epithelization. The "closed plaster" versus the "open" treatment of wounds.—Under plaster the wounds received complete immobilization and adequate pressure which appeared to control systemic infection and favour local circulation. Local infection was not controlled as evidenced by the purulent exudate containing a rich and varied bacterial flora.

The closed plaster appeared to be highly favourable to the connective tissue repair of the wound. It was a constant surprise at the change of plaster to see the healthy-looking granulations under the pus. It did not, however, seem to favour epithelial regeneration, which was very slow, some wounds after months in plaster showing little new epithelium. The epithelium furthermore appeared of poor quality and thin, and could easily be wiped away with gauze.

Generally speaking, the wounds that did heal well under plaster appeared to do so by maximal contraction and by minimal epithelization. It was therefore thought that the stagnation of purulent exudate is unfavourable to epithelial growth.

Attempts were made to dress the wounds of compound fractures through windows cut in the plaster. This method proved unsatisfactory. Local œdema occurred in the wound, it was found difficult to keep the area surrounding the wound clear, and exudate tended to diffuse under the plaster; often to expose the wound adequately it was necessary to cut a window so large as to menace the stability of the fixation.

Furthermore, wounds presenting skin losses were observed under plaster, when because of their unfavourable anatomical position and of the extent of the skin loss, epithelial healing could only take place, if at all, after a long time interval. During this time the increasing fibrosis would be such as to impair seriously the circulation of the limb by constriction, and produce a wound healing of poor quality destined to break down repeatedly.

Other cases were observed in which unhealed superficial tissue losses under plaster delayed the performance of important secondary surgery on the bones, the nerves or the tendons.

It became evident that in such cases great benefit would be derived from successful skin grafting of the wounds.

Secondary skin grafting in compound fractures.—Wounds were observed when the plaster was changed. Cultures were taken. If grafting was indicated, plans were made for grafting at the next change of plaster.

At this time, after removal of the plaster a thorough washing of the wound and surrounding skin was done, removing all exudate and dried pus and crusts. A skin graft was then taken from one of the thighs.

Total excision of the wound was performed down to healthy muscle. Sulphanilamide powder was applied with Pearce's insufflator and the skin graft immobilized with pressure. A plaster cast was then reapplied to the extremity. On removal of the plaster from four to six weeks later it was found that the graft had taken in a proportion of from 70% to 100%.

Six wounds under plaster were grafted in this manner. Two were infected with type A hæmolytic streptococcus and the operation was performed in presence of this organism, local chemotherapy was used and a course of oral sulphathiazole was given for five days. Two were infected with pyocyaneus. This organism was not found after the operation. Two cases presented staphylococci only.

This method of skin grafting wounds of compound fractures interferes in no way with the routine closed plaster treatment. It brings, however, to this method of treatment the one element in which it appears deficient, epithelium.

Secondary skin grafting in compound fractures treated by external skeletal pin fixation.—In such cases the wounds can be treated by local chemotherapy and other methods under conditions similar to those found in skin grafting open granulating wounds, described above.

Primary excision. Primary skin grafting.—The most opportune time to provide the wound with a skin covering would appear to be at the time of the primary excision. After removal of all the devitalized tissue and of foreign bodies, sulphanilamide powder is blown into the resulting saucer-shaped wound in a thin even layer, and a skin graft is laid into the wound and held in position by the firm even pressure produced by cotton-wool or sponge. The plaster can be applied immediately over this dressing or a bandage including not only the wound area but the whole limb can be used for fixation before application of the plaster.

The compound fracture is then treated by the closed plaster method, the plaster being changed at the desired time interval. The skin grafting has in no way interfered with the

routine closed plaster treatment, but adds to this method the great advantage of an epithelized wound.

Primary excision. Late primary skin grafting.—Under the stress of conditions prevailing at the time the patient is received at the hospital (air raid) in order to save time it may be preferable to perform the primary excision, apply the local chemotherapy in the form of sulphanilamide powder or a gauze dressing saturated with the drug in the wound, apply the plaster and postpone the skin grafting until more time is available; it is possible that the tenth day may be the most suitable time for this procedure. The plaster is removed and a skin graft is applied.

Types of skin graft used.—The most suitable graft is the " thick razor " graft, also called the " intermediate " or " split " graft. It is cut with the Blair skin graft knife usually from the lateral or medial aspects of the thigh. This graft is thicker than the Ollier-Thiersch. The latter graft because of its thinness has a slightly higher degree of " take ". It is, however, less resistant to functional stress than the intermediate graft which gives a strong epithelial covering that in most cases will be permanent.

The " pinch-graft " (Davis) is not suitable in the type of repair considered. It gives an epithelization by " second intention ", the epithelium spreads out from the individual islands that are grafted. The " pinch graft " is valuable in extensive burns. We are not, however, concerned with this type of injury in this paper but rather with the more localized tissue loss in which the best result can be obtained when the " sheet " type of graft, if placed under suitable conditions, will take *per primam*.

Removal of a razor graft requires some practised skill. Two recent additions to the surgeon's armamentarium have rendered the removal of skin grafts easier, the dermatome (Padgett) and the calibrated razor knife (Humby).

The thickness of the graft should vary from 8/1000 to 14/1000 of an inch, as calibrated by the Padgett dermatome.

The graft can be spread over tulle gras or vaseline gauze (Gillies) before being applied over the wound. If multiple pieces of graft are needed they are laid on the tulle gras slightly overlapping so as to form a continuous epithelial covering.

Covering of bone and tendon.—Skin grafts are not successful over bone deprived of periosteum although they will take well on the latter membrane. They are usually unsuccessful over tendon deprived of its sheath. In such cases it is necessary to cover the exposed structures with a flap of skin, subcutaneous tissue and fat cut from the side of the extremity and transposed over the defect. The wider this flap is made the better its blood supply. Care should be taken, particularly in the frequently used method of covering a tibial defect by flaps created by parallel incisions. These flaps when made long and narrow will become devitalized.

Avulsed flaps.—Large avulsed flaps when they present a wide base may be successfully sutured back into position. If the base appears insufficient to ensure its adequate blood supply it is preferable to remove all the fat until the base of the corium is exposed, thus realizing a full-thickness graft over which adequate pressure is applied as for a free graft.

CONCLUSIONS

Extensive loss of skin leads to fibrotic and inflammatory changes in wounds of the extremities. Late complications, contractures, constrictions, unhealed wounds necessitating secondary operations often delay the patient's return to active work.

Wounds of the extremities presenting extensive skin losses should be treated by a primary skin graft dressing if possible.

Failing this procedure secondary skin grafting should be carried out at the earliest moment.

Chemotherapy has made possible the grafting of infected wounds following secondary excision with a successful result in 88% of cases.

Cases shown by Doctors DONALD E. DIAL, DUDLEY SMITH and NORMAN EGEL

(1) Infected compound fracture of humerus involving elbow-joint immobilized by Haynes pin fixation.

(2) Simple fracture of humerus immobilized by Roger Anderson pin fixation.

(3) Fracture of clavicle treated by fixation with Kirschner wires and immediate mobilization of shoulder.

(4) Fracture of metacarpal immobilized by Waknitz pin fixation method.

(5) Wire fixation for hammer toe correction.

(6) Skin graft operations on combined orthopædic and plastic cases.

Section of Obstetrics and Gynæcology

President—W. Gilliatt, C.V.O., M.S.

[*April* 19, 1940]

(*Other Material from this Meeting was Published September* 1940)

A Case of Osteomalacia

By Meave Kenny, M.R.C.O.G.

(*From the Department of Obstetrics and Gynæcology of the British Postgraduate Medical School*)

Mrs. G. Singh, aged 22, a native of the Punjab, came to England in January 1933 with her husband, a poor street trader.

First pregnancy in 1936, not complicated, and resulting, after an eleven hours' labour, in the full-time normal delivery of a 5½ lb. living male child, S. Singh.

Second pregnancy in 1939. The woman attended the Medical Out-Patients' Department in March, when ten weeks pregnant, complaining of pain in hips, thighs, knees, and shoulders. These symptoms had been present for six months, and opacities had appeared in both eyes about a year before. Trachomatous deformities of the eyelids and pannus were present, with active ulceration of the left cornea. K 2-3/28 menarche at 14 years of age.

The patient was admitted to hospital. She used to sit with knees drawn up, or lie on the right side, curled up and in great pain. She had limitation of abduction of both hips, and movements of all lower limb joints were painful and limited. Left genu valgum and wasting of the quadriceps were present. There was an absence of lumbar lordosis and the trunk appeared shortened (fig. 1). The uterus, enlarged to the size of a grapefruit, was perched above the rostrate pelvic brim, and reached almost to the umbilicus. Radiography displayed typical osteomalacic deformities of the pelvis, with patchy rarefaction of the bones simulating fractures of the pubic rami and alæ of the ilium (fig. 2), and of the left fibula. The vertebral bodies were somewhat flattened.

Blood chemistry.—23.3.39:	Serum calcium	13·4 mg. per 100 c.c.
	Plasma phosphates	3·1 „ „ „ „
	Plasma phosphatase	18 units „ „ „
17.4.39:	Serum calcium	11·4 mg. per 100 c.c.
	Plasma phosphates	2·5 „ „ „ „
	Plasma phosphatase	16 units „ „ „
4.5.39:	Serum calcium	11·2 mg. per 100 c.c.
	Plasma phosphates	3·1 „ „ „ „
	Plasma phosphatase	22 units „ „ „
Treatment begun.—Radiostol: 30,000 units daily and ordinary diet.		
4.6.39:	Serum calcium	9·7 mg. per 100 c.c.
	Plasma phosphatase	24 units „ „ „
Treatment continued.—Radiostol: 15,000 units daily and high calcium diet. W. R. and Kahn negative. Hb. 92%. (Calcium excretion: 120 units in three days—normal)		

During three months in hospital the clinical condition improved greatly, although the X-ray appearances of the bones did not change. Her attendances at the antenatal clinic were irregular, but her health continued good with haliverol and calcium. In the rush of events towards the end of August 1939 the woman was swept away into the country with her little son and we found her with some difficulty. But she was now happier than she had been since reaching England. The Government evacuation scheme allowed her comfortable billets and more money than her husband had ever

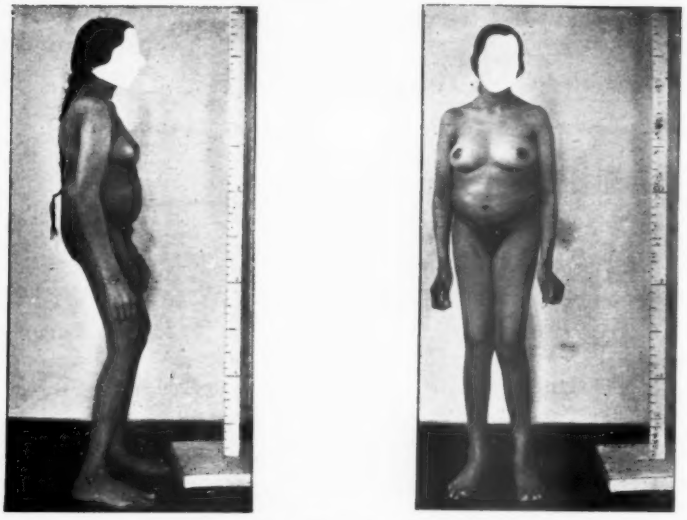


FIG. 1.—Showing absence of lumbar lordosis, adduction of thighs and left genu valgum; also abnormal height of fundus at third month of gestation.

FIG. 2.—25.3.39: Showing typical osteomalacic deformities with patchy rarefaction of pubic rami and ilium simulating fractures.

earned. She was loath to return to London for her confinement in case she endangered these benefits, and so adopted a non-co-operative attitude. She was admitted to the High Wycombe Hospital in labour on October 14, with evidence of gross disproportion between presenting part and pelvis. Cæsarean section was performed by the consulting surgeon, and a living girl, S. Kour, weighing 5 lb. delivered. Recovery was good. She revisited the British Postgraduate Medical School in March 1940. She described herself as being in excellent health, although the trachomatous condition of her eyes was again active and fresh corneal ulcers had appeared.

We persuaded the girl to enter hospital once more for further investigation of her deficiency and treatment of herself and her baby. Radiography showed almost complete healing of the pseudo-fractures of pelvic bones and fibula (fig. 3).

Blood chemistry.—15.4.40: Serum calcium 12·0 mg. per 100 c.c.
Plasma phosphates (as P.) 2·6 „ „ „ „
Plasma phosphatase 22 units „ „ „

FIG. 3.—13.4.40: Showing healing of the areas of rarefaction seen in fig. 2.

Comment.—There is evidence to show that a calcium and phosphorous deficiency in the diet of the pregnant woman, or a deficiency of either, predisposes her child to rickets. In cases of extreme deficiency rickets may even be present at birth (Preston Maxwell, &c., 1934, 1939). It is probably more common to find the child born with a predisposition to rickets, a predisposition which is not always capable of being overcome by good postnatal feeding. Mellanby (1933), experimenting with dogs, showed in the young of deficient bitches that this tendency to rickets *is not removed by a period of good diet* and may become evident at a later period.

The first child of my patient, S. Singh, is now 3½ years old and shows marked dental caries and X-ray evidence of healed rickety lesions of the tibia. It was never nursed by the mother, but fed on a well-known brand of vitaminized dried milk. It has frequent respiratory tract infections and is underweight for its age.

The second child, S. Kour, now 6 months old, is an apparently healthy and well-nourished baby, weight 14 lb., but X-rays show it to have signs of active rickets.

Blood chemistry (S. Kour).—Serum calcium		15·2 mg. per 100 c.c.
	Plasma phosphates	3·2 „ „ „ „
	Plasma phosphatase	23 units „ „ „
	Hb. 100%	

It has been fed since birth on vitaminized dried milk supplied by the local infant welfare authorities. Breast feeding was not attempted, so the question of calcium deficiency of the mother's milk does not arise.

The interest of this case is in the fact that the patient appears to have developed this disease in England. She is of an Indian religious sect, the Sikhs, in which rickets and osteomalacia are rare because of their mixed diet of milk products, meat and vegetables and open-air life. In the Punjab, the disease is prevalent among Mohammedan women of all classes who observe strict *purdah*, and among only the poorest class of Hindus whose diet is of good quality but grossly insufficient quantity. The clinical type of this case corresponded to Green-Armytage's Class III (1936), the most prominent symptoms being the rheumatic pains about shoulder girdle, thigh and back.

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[*May* 16, 1941]

Experience with the Intravenous Use of the Follicle-Stimulating Hormone of the Anterior Pituitary in Menstrual Disorders

By MEAVE KENNY, M.R.C.O.G., and DOREEN DALEY, M.D.

(*From the Department of Obstetrics and Gynæcology of the British Postgraduate Medical School*)

IN the last decade there has been much investigation and therapeutic trial in menstrual disorders of endocrinal origin.

Treatment has followed many lines. In metropathia hæmorrhagica and ovulatory menorrhagia, removal of the bleeding surface, injection of luteinizing hormones and the induction of temporary amenorrhœa with testosterone have been usually only of temporary value; and, except where there is a well-marked thyroid deficiency, endocrine therapy has had little permanent success in cases of amenorrhœa.

Recently attempts have been made to treat the conditions by the use of gonadotrophic hormones. Follicle-stimulating anterior pituitary hormone derived from the serum of pregnant mares has been injected intramuscularly over a period of a fortnight, followed by luteinizing hormone in the succeeding fortnight, and continued for a few months. Though there was an occasional temporary improvement in symptoms in cases of metropathia hæmorrhagica treated in this way, relapse was frequent, and cases of amenorrhœa seemed to derive no benefit from this form of therapy. In fact, gynæcologists seem to find little use for gonadotrophic hormones, save in the treatment of threatened abortion.

Within the last few years encouraging reports have come from the United States of America following the *intravenous* administration of follicle-stimulating hormone. Davis and Koff [1] have had good results with such treatment in sterile women with anovulatory cycles, and have had some response in amenorrhœa resulting from inadequate ovarian activity.

Through the generosity of a firm of Dutch chemists (Organon Ltd.) working in this country, we have been able to test the efficacy of a follicle-stimulating hormone, known as Gestyl, derived from pregnant mares' serum, which is suitably prepared for intravenous therapy. We describe here the clinical effect, and, as far as possible, the response of the

ovary as shown by histological examination of endometrial curettings. The routine dosage we have used is 500 units of Gestyl, given intravenously, on three successive days in mid-cycle. In all cases we have tested for serum sensitivity before giving the full dose into the vein, and have had no untoward reaction, except for a rigor in one patient who was developing an acute febrile disease manifest the next day.

The series is small. Follow-up has been very difficult owing to evacuation of patients from London, and some cases, especially the successful ones, have been unwilling to lose time from work, or leave evacuation centres to come up for endometrial biopsy, so that we have had to compile their later history from letters only.

The cases treated fall into three groups: (1) Metropathia hæmorrhagica; (2) menorrhagia with ovulation; (3) secondary amenorrhœa.

CASE HISTORIES

(1) *Metropathia hæmorrhagica* (4 cases).

(A) Mrs. M. A., aged 23, nulliparous, a commercial artist, first attended in January 1940.

History.—Menarche 13½, cycle 4-5/28 until May 1939, when her husband left her after a quarrel. She then had five weeks of heavy vaginal bleeding. The cycle was

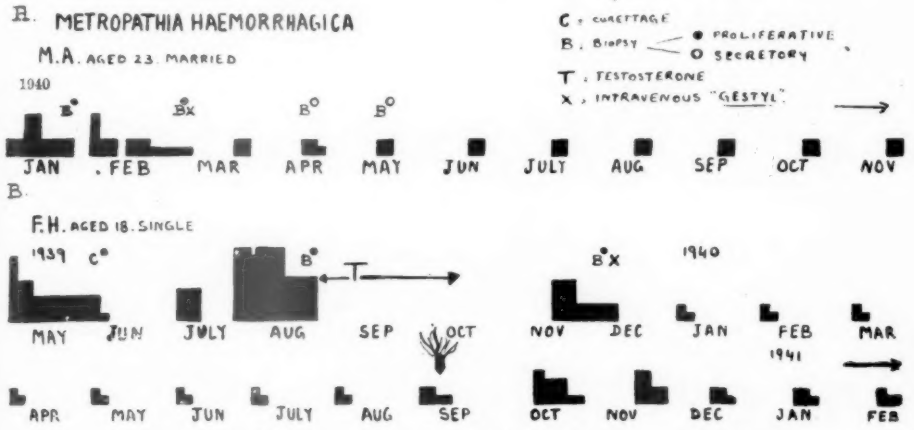

FIG. 1.—The blocks represent the duration and amount of bleeding.

resumed, 10-14/28, until January 1940, when, after eight weeks amenorrhœa, she lost heavily for four weeks. Biopsy of the endometrium then, and six weeks later after further profuse bleeding, showed the typical picture of metropathia hæmorrhagica.

Examination.—No gross abnormality; Hb. 60%.

Treatment.—500 units of Gestyl by the intravenous route on three successive days in March 1940.

Result.—Thirteen days later a normal period began. Endometrial biopsy on the first day showed a well-developed secretory phase. Cycle 6-7/28 ever since.

(B) Miss F. H., aged 18, nulliparous, a shop assistant, first attended in May 1939.

History.—Menarche 13, cycle 6/28 until May 1938. The periods then became irregular and heavy, lasting two to three weeks with only one to two weeks' free interval. After seven weeks' bleeding, only slightly diminished by large doses of Progesterone, the uterus was curetted under anæsthesia. The endometrium showed hyperœstrinization. Heavy bleeding recurred in July and August when biopsy again showed a persistent œstrin effect on the endometrium. Testosterone was given in 100 mg. daily doses, up to a total of 1,000 mg., and in the confusion attending out-patient treatment at the beginning of the war, the patient continued to have injections without advice until a total dosage of 3,800 mg. was reached! Three months' amenorrhœa, acne and hoarseness resulted, followed by three weeks' irregular bleeding, and the endometrium again showed metropathic changes.

Examination.—No gross abnormality; Hb. 54%.

Treatment.—500 units of Gestyl intravenously on three successive days in December 1939.

Progress.—Fourteen days after the third injection, a normal five-day period started. A regular 5/28 cycle continued until the beginning of September 1940, when heavy bombing of the patient's home district resulted in the production of five weeks of amenorrhœa followed by two weeks of continuous bleeding. Since then, the cycle has resumed a regular rhythm. It has not been possible to obtain endometrial evidence of ovulation, as the patient is unable to attend hospital, and her history following injection of Gestyl has been supplied by her sister, who has been under prolonged treatment for the same condition of metropathia.

(C) Miss L. B., aged 30, nulliparous, shop assistant, first attended October 1939.

History.—Menarche 14. Cycle 4/28-35 until the age of 23. The patient nursed her mother during a trying illness which interfered with her marriage plans and then had

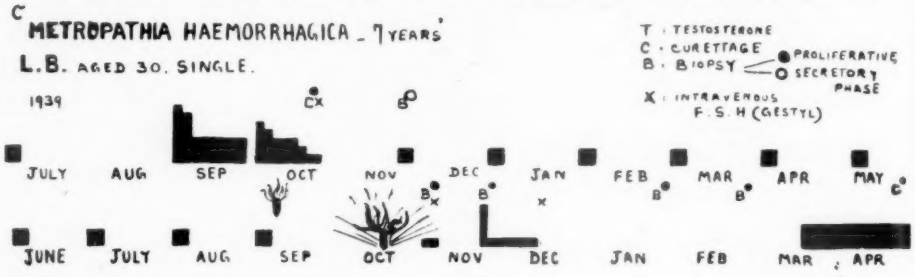
C
METROPATHIA HAEMORRHAGICA - 7 YEARS
L.B. AGED 30. SINGLE.
T : TESTOSTERONE
C : CURETTAGE
B : BIOPSY
PROLIFERATIVE
SECRETORY PHASE
X : INTRAVENOUS F.S.H (GESTYL)
1939
JULY AUG SEP OCT NOV DEC JAN FEB MAR APR MAY
JUNE JULY AUG SEP OCT NOV DEC JAN FEB MAR APR
D.
METROPATHIA HAEMORRHAGICA - 9 YEARS.
M.H. AGED 24. MARRIED.
R : X-Rays.
1940
JAN FEB MAR APR MAY JUNE JUL AUG SEP OCT NOV
R

FIG. 2.—The blocks represent the duration and amount of bleeding. The diagrammatic "bombs" represent contemporary events related to ætiology and amplified in text.

three months' amenorrhœa followed by six weeks' continuous bleeding from the uterus. During the next seven years she had heavy irregular periods only temporarily relieved by curettage of the uterus and much hormone therapy at other hands.

Examination.—A thin, exasperated woman. There was no palpable pelvic disease. Curettage of the uterus was performed. The endometrium was polypoid and showed histological changes typical of metropathia hæmorrhagica.

Treatment.—She was given 500 units of Gestyl intravenously on three successive days after curettage, in October 1939.

Progress.—Twenty-eight days after the third injection, an endometrial biopsy was taken and showed a well-marked secretory phase. On the next day, a normal period started. Regular five-day periods occurred every four weeks in the following eleven months. A second menstrual biopsy during this time showed also a well-marked secretory phase. In September 1940 she had her last normal period. Heavy air raids on London began and the patient's timid disposition was grievously affected. Her home was bombed in October and, after eight and a half weeks' amenorrhœa, she once more attended the clinic. A biopsy of the endometrium was taken which showed persistence of the œstrin phase. She was given a second course of Gestyl. Eighteen days later, she started to bleed and continued to do so for three weeks. Endometrial biopsy on the first day of this loss again showed an exaggerated œstrin phase. A third course of Gestyl was given and she had no further bleeding for the next fourteen weeks. Two biopsies taken at twenty-eight-day intervals after the last injection showed no change

in the endometrium. In the middle of March heavy bleeding started and continued until she was admitted for curettage four weeks later. Bleeding persists after curettage, although it is lessening now, three weeks after. Curettings showed the typical appearances of metropathia hæmorrhagica once more. X-ray therapy is being considered.

(D) Mrs. M. H., aged 24, nulliparous, first attendance April 1938.

History.—Menarche 13, cycle 7/28-31 for a year, after which it changed to 7-21/14-21. Dilatation and curettage, Progesterone, intramuscular follicle-stimulating hormone alternating with luteinizing hormone, and Testosterone, have been followed by not more than a month's relief at any time, and marriage caused no improvement.

Examination.—No abnormality was found on examination except for pallor (Hb. 62%). Endometrial curettings were polypoid and showed changes characteristic of metropathia hæmorrhagica.

Treatment.—500 units of Gestyl intravenously on three successive days in April 1940.

Progress.—Eight days of bleeding occurred ten days after the third injection. Five and a half weeks later bleeding started again and lasted a fortnight. A course of Testosterone, 10 mg., on alternate days for 10 doses was given but bleeding followed for eleven days. A further intravenous injection of 500 units of Gestyl was given, preceded by three daily intramuscular injections of 100 units of follicle-stimulating hormone (Antostab). A normal period followed three weeks' amenorrhœa. Ten days later excessive bleeding started and persisted for three weeks. A third course of Gestyl in the third week was ineffective. A subcastration dose of X-rays has been given and amenorrhœa has resulted.

(2) *Menorrhagia with ovulation* (2 cases).

(E) Mrs. N. C., aged 34, nulliparous, first attendance November 1938.

History.—Menarche 15, cycle 5/28 until the age of 26, when she had six weeks' continuous bleeding. The cycle was regular for the next year and then periods became completely irregular with heavy bleeding for as long as three months at a time. When she attended the Out-patient Department in November 1938, it was after five weeks of continuous heavy loss. This and subsequent heavy irregular periods were controlled to some extent with Progesterone, until May 1939. Then the cycle remained 15/26-28 for five months, becoming irregular with excessive loss once more until her visit in December 1940.

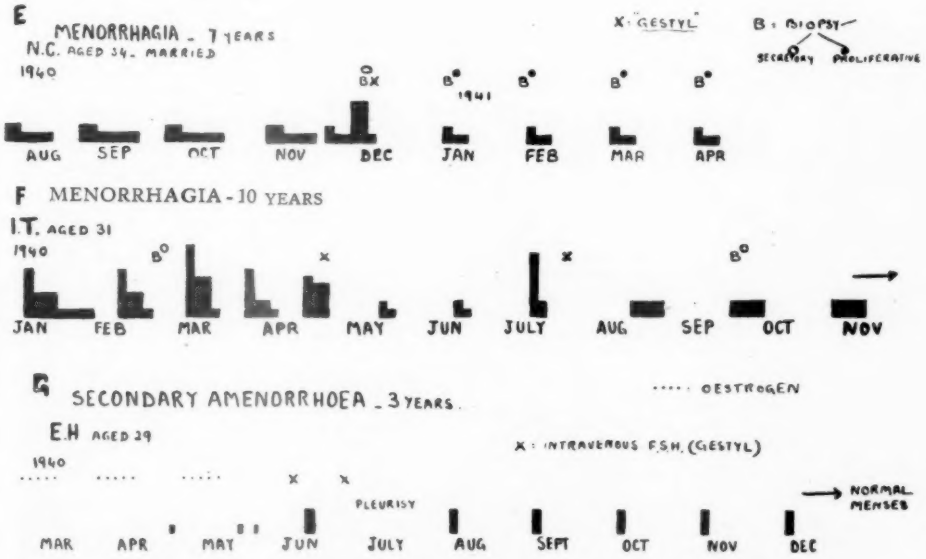

FIG. 3.—The blocks represent the duration and amount of bleeding.

Examination.—The genital tract appeared to be normal, endometrial curettings on the twentieth day of the cycle were scanty but showed some evidence of a secretory phase.

Treatment.—500 units of Gestyl intravenously on three successive days in December 1940.

Progress.—Eighteen days after the third injection a period started which lasted nine days. Endometrial biopsy on the first day showed persistent œstrin phase. Thirty-one days after the beginning of this period there was bleeding for six days in March. Again there was no evidence of a secretory phase in the endometrium examined. A 6/28 day cycle is now established, but in view of her previous history and the present non-ovulatory appearances of the endometrium, a guarded prognosis must be given (fig. 3).

(F) Mrs. I. T., aged 31, nulliparous, first attendance July 1937.

History.—Menarche 16, cycle 7-8/28, until appendicectomy at the age of 21 when the cycle changed to 10/14-21. Curettage eight years later was followed by a 4-5/28 cycle for the next seven months, but relapse then occurred and the cycle became 10-14/14-21 days for the two years before she attended this clinic. The loss was heavy enough to force her to rest in bed for several days during each period.

Examination.—Examination showed a thin, pale, depressed woman, Hb. 60%. Endometrial curettings were profuse, and on the seventeenth day of the cycle showed early secretory phase. The cervix was cauterized. During the next seven weeks, heavy bleeding occurred on four occasions.

Treatment.—500 units of Gestyl intravenously on three consecutive days in April 1940.

Progress.—Thirteen days after the course a nine-day period started. Unfortunately, the patient was unable to attend hospital for biopsy on this occasion, or, twenty-eight days later, when she started a second nine-day period heavier than the first one. Three weeks later she was confined to bed on account of a six days' "flooding" and so, on her next attendance eight days later, a further course of follicle-stimulating hormone was given. This time 100 units of Antostab were given intramuscularly on three consecutive days, followed by one intravenous dose of 500 units of Gestyl. Three weeks later a period started, and a 12/28 day cycle has continued ever since. The patient is able to go about her duties now, as the periodic loss, though prolonged, is regular and not excessive in amount, and the free interval is longer. A menstrual biopsy shows that ovulation occurs as before treatment, and the patient has been advised to court pregnancy (fig. 3).

(3) *Secondary amenorrhœa* (3 cases).

(G) Miss E. H., aged 29, nulliparous, shop assistant, first attendance January 1940.

History.—Menarche 18, cycle 4/35-42 until the death of her mother three years later, when the cycle changed to one day's loss about every three months. This continued for five years, and was followed by complete amenorrhœa for three years, except for occasional slight loss during courses of œstrin given elsewhere.

Examination.—A pale, thin, woman without any gross abnormality. Under anæsthesia a scanty endometrial fragment was obtained from a uterus 2 in. long, and showed atrophic glands.

Treatment and progress.—Œstrin was given during the first half of the following three months, in order to bring about endometrial proliferation. Œstradiol benzoate 50,000 units on alternate days was used as there was intolerance to synthetic œstrogens. There was slight œstrin withdrawal bleeding in the second and third months. In the middle of the fourth month, June 1940, she was given 500 units of Gestyl intravenously on three successive days. A week later she had fairly heavy bleeding for two days. In the next week she had another course of Gestyl. This was followed by a slight rigor which may have heralded the development of a pleurisy a day later; but following this, she had short but regular monthly periods, 3/28. These continue, according to information received by letter. The patient is occupied in national service and we have not been able to perform endometrial biopsy to confirm ovulation (fig. 3).

Miss J. A., aged 19, first attendance April 1940.

History.—Menarche 14, cycle 5-14 until age of 16 when she left school and began work as a bank clerk. During the next year periods occurred every three weeks until their sudden cessation in August 1938. She had then some impairment of general health with anorexia and lassitude possibly due to night study in addition to her daily bread-winning employment.

Examination.—A tall, intelligent, artistic type of girl with long slender limbs. Her hair was dry but luxuriant, and there was slight facial hirsuties. There was no evidence of general disease. Hb. 90%.

Special examination.—B.M.R., sugar tolerance test and X-ray of pituitary fossa showed no gross abnormality, closure of epiphyses was normal for her age. On examination under anæsthetic, the uterus was found to be anteverted, of adult type, and the

cavity 2½ in. long. There was no evidence of adnexal disease. The endometrium was atrophic and it was not possible to obtain by curettage sufficient material for histological examination.

Progress.—She was started on a three months' course of Stilbœstrol, 1 mg. daily, alternating fortnightly with oral Progesterone, 2 mg. daily. She had slight bleeding for one day in the fifth week only. In the fourth month of treatment she was given 100 units of follicle-stimulating hormone (Antostab) intramuscularly daily for three doses followed by 500 units intravenously of Gestyl. There was no response to treatment. Stimulating doses of X-rays to the ovaries have been given without effect.

Miss A. B., aged 24, a typist, first attendance March 1939.

History.—Menarche 12, cycle 7/28 until the age of 19, when she dieted herself excessively in order to lose weight. This loss was stated to be of nearly 4 st., and the girl was in bed for six months, recovering.

Examination.—Examination showed an attractive, healthy girl weighing 8½ st. The external genitalia were normal. The uterus was of adult type, 2½ in. long but flabby and thin-walled. Endometrium was not obtainable by curettage, being markedly atrophic.

Progress.—Throughout the next year she was given various œstrogens, and finally a course of intramuscular follicle-stimulating hormone (Antostab). There was occassional very slight œstrin withdrawal bleeding but loss did not occur spontaneously on any occasion. At the end of a fourteen days' course of Stilbœstrol, 5 mg. daily, she was given 500 units of Gestyl intravenously on three successive days in April 1940. There was no response to this treatment, and we have not seen the patient again as she is in the Auxiliary Territorial Service.

TABLE I.

EXPERIENCE WITH THE INTRAVENOUS USE OF THE FOLLICLE STIMULATING HORMONE (GESTYL) OF THE ANTERIOR PITUITARY IN MENSTRUAL DISORDERS.

NAME & Hospl.No.	AGE	DURATION of disease	OTHER TTMT. Result.	"GESTYL" Result.	REMARKS.
METROPATHIA HAEMORRHAGICA.					
Mrs.E.A.	23	3 months	none	Cure	Regular periodsfor 13 mths
Miss F.H.	18	2 years	Curettage & Testosterone 8 relief	Cure	" " " 11 mths
Miss L.D.	30	7 years	Curettages (3) & 3-4 ms.relief only.Progestin temporary effect.	Cure	Immediately following 4th. curettage,GESTYL given. 13 mths regular periods until homo bombed,now rolapse
Mrs.M.H.	24	9 years	Curettages (2) Testosterone, Progesterone, A.P.H.(1.m.)each gave 1-2 ms.relief	No effect	Severe secondary anaemia. Amenorrhoea induced with small doses X-rays.
MENORRHAGIA.					
Mrs.N.C.	34	7 years	Progesterone,no relief.	Relief	Ovulatory bleeding.No ovulation since GESTYL,but periods regular with moderate loss.
Mrs I.T.	31	10 years	Curettages (2) with 2-3 ms. relief.	Relief	Periods regular,loss much diminished but still some what excessive.
SECONDARY AMENORRHOEA.					
Miss E.H.	29	3 years	Oestrogen for 3 mths.causing slight bleeding	Cure	Regular cycle 3/28 for last 11 mths.except during attack of pleurisy.
Miss J.A.	19	3 years	Curettage,oestrogen for 3 months no result.	No effect	Atrophic endometrium. No effect after stimulating dose of X-rays to ovary.
Miss A.B.	24	5 years	Curettage,oestrogen withdrawal bleeding (3)	No effect.	Atrophic endometrium

SUMMARY OF RESULTS (TABLE 1)

(A) *Metropathia hæmorrhagica.*—Regular menstruation has been induced in three of four cases; in two of these cases ovulation was definitely produced, and it is possibly occurring in the third case also. There has been complete failure after repeated efforts in one case, and one of the successful cases has relapsed after thirteen months' relief. It is possible that these two women have acquired a specific resistance to pregnant mare's serum and are now intractable by this means.

All but one case had been treated by other methods, without relief, before receiving Gestyl.

(B) *Menorrhagia with ovulation.*—Gestyl has been of doubtful value in these two cases. There has been definite clinical improvement, the irregular prolonged menstrual loss becoming regular and moderate in amount. The nature of the ovarian response is ambiguous.

(C) *Secondary amenorrhœa.*—One of three cases has responded satisfactorily to Gestyl therapy and is menstruating regularly. Biopsy to confirm ovulation has not been possible.

There has been a marked association of "psychic trauma" with the onset of menstrual disturbances, or with relapse after apparent cure. Domestic strain, disappointment in love, and, recently and vividly, the bombing of homes seem to play havoc with an unstable endocrine system (figs. 1 and 2).

No explanation is offered for success or failure in these cases. The results are as yet inconclusive and long follow-up will be necessary before they can be finally evaluated, but they appear to be sufficiently encouraging for other gynæcologists to give an extended trial to follicle-stimulating hormone by the intravenous route in appropriate cases. Control by estimation of hormonal secretion which has unfortunately not been available in the present circumstances would be of great interest.

These cases are published with the permission of the Chief Medical Officer of the London County Council.

Reference.—1 DAVIS, M. E., and KOFF, A. K., Experimental Production of Ovulation in Human Subjects, *Am. J. Obst. & Gynec.* (1938), **36**, 183-199.

Endometrioma of the Colon Causing Stricture.—J. B. BLAIKLEY, F.R.C.S.

This specimen is part of a pelvic colon which I removed in 1940. It shows an annular stricture from endometriosis. The patient was a single woman, stout, aged 40, who gave the following history: she had always had dysmenorrhœa with pain in the left iliac fossa, but it had got worse recently. When I saw her she had pain in the hypogastrium for a week before a period, severe pain during the period, and colicky pains at other times, also she frequently vomited. During an attack of pain she got constipated and latterly during a period had extreme difficulty in procuring an action of the bowels; when they did act she noticed that one side of the stool was distinctly flattened. Examination showed the uterus to be slightly enlarged and that there was a tender nodule on the back of the uterus. I diagnosed endometriosis and on May 14, 1940, I did a laparotomy in the Chelsea Hospital for Women. I found bilateral endometriomata of the ovaries and extensive endometriosis of the pouch of Douglas. I did a subtotal hysterectomy and removed both ovaries. On examining the pelvic colon I found that the middle of the loop, which had been lightly adherent in the pelvis, showed an annular stricture, and that the wall of the bowel above was markedly hypertrophied. I did a Paul's operation and exteriorized the affected colon through an incision in the left iliac fossa. Subsequently the spur was clamped and the resulting fæcal fistula was later closed.

In the literature there is little reference to endometriosis of the colon causing severe stricture. Like others I have been familiar with puckering caused by isolated masses, but never complete encirclement of the bowel. After removal, examination of the specimen showed that it was not possible to get the tip of the little finger through the stricture and it was seen that the mucous membrane was freely movable over the fibrous tissue which composed the stricture and which felt like cartilage. Microscopical section showed typical islets of endometrium here and there in the fibrous tissue.

Section of the History of Medicine

President—Sir Walter Langdon-Brown, M.D.

[*June* 11, 1941]

The Royal College of Physicians of London, on the Occasion of its Recent Bombing

By A. P. Cawadias, O.B.E., M.D., F.R.C.P.[1]

One night in November 1940 a high explosive bomb fell through a skylight in the library of the Royal College of Physicians. The College had already been damaged in October, but the November hit was the more destructive. Half the library was open to the sky, the floor at the point of penetration was found to be sagging, blast blew the glass from the bookcases, and hundreds of books were scattered. The force of the explosion was demonstrated by the small metal fragments which were found embedded in a few of the volumes. Fortunately precautions had been already taken for the most valuable books from the XVI and XVII century (pre the Great Fire) collections and for the Dorchester and Lloyd Roberts bequests. Among the remainder there was surprisingly little damage, although most of them were covered in white dust from fallen plaster. A few volumes were cut by glass. Others lost leaves which were carefully salvaged.

However, the damaged roof was a great danger to the books. With the assistance of the Royal Society of Medicine's staff, the staff of the College were able to remove the volumes, which were sent to the Secretary's house to be stored. They were removed just in time to save them from damage by heavy rain.

Thus the damage to the building was great but not for the moment irreparable. The books were saved, and some of them are those that survived also the Great Fire of 1666. Materially the College has not suffered extensively, but the bombing is a symbol for those who think historically, and stimulates us to this way of thought. We can understand an actual situation only by considering all that has led up to it, and we must think in this way as an essential preparation for action.

General development of the colleges of physicians

College in Roman law means corporation, and the object for which colleges or corporations of physicians were formed,in the early Middle Ages was the regulation and administration of medical practice. The College of Physicians of Rome, existing in the very early Middle Ages, was composed of a dozen doctors, all of genuine Roman family and education, who exercised a kind of surveillance over all who professed the art of curing —physicians, barbers, surgeons, apothecaries. Any who wished to practise these crafts had to submit to an examination before the College, and had also to show that they were not afflicted by any infirmity of a nature to render them ridiculous or objectionable and that they had never committed a "voluntary homicide". This College corresponded thus to the Fellowship of the contemporary Colleges of Physicians. Vacancies among the members were filled by co-option among the other Roman physicians [1].

[1] I should like to acknowledge the help of Mr. H. M. Barlow, the Secretary of the College, who gave me all details of the bombing.

FIG. 1.—The Library after the bombing.

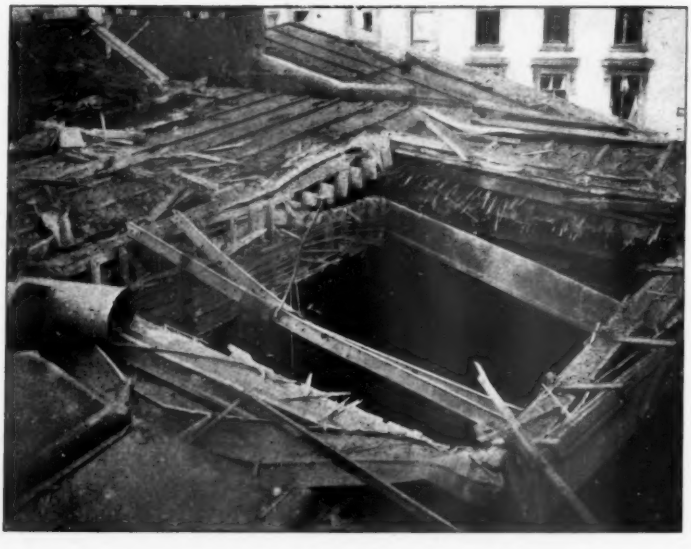

FIG. 2.—The roof of the College after the bombing.

In place of the Roman colleges the Germanic peoples had guilds. In Florence, for instance, there was a powerful guild of physicians and apothecaries in the thirteenth century. It was a corporation of all Florentine physicians and apothecaries and thus had a monopoly of healing practice. Incorporation was obtained after examination, obligatory even to University graduates. The powers of the guild were vested in four consuls who constituted the examining as well as the general governing and organizing body of medical practice. It is believed that the consuls were elected by the vote of all the guild members.

In Roman colleges as well as Germanic guilds, dinners, festivities, religious and other ceremonies played an important rôle, and many of our modern colleges have ceremonies which can be traced to that remote origin. It is interesting to speculate upon the relation of our four censors to the four consuls of the Florentine guild.

During the pre-Renaissance and Renaissance, colleges of physicians were founded in Italy, combining the natures of the Roman colleges and the Germanic guilds. For each particular town a corporation of physicians had the monopoly of practice. Like the Roman colleges the governing and examining body of the corporations was formed of the most eminent of their members, the socii or fellows. These new colleges had as their object the organization and administration of medical practice in a certain town or region, and to that effect they exerted academic, administrative and medico-political functions, all vested in the fellows. The academic functions consisted in teaching, and principally in examining for award of the special diplomas which permitted incorporation into the college and thus practice in that particular area, licences which even University graduates had to obtain. The administrative functions consisted in supervising the medical practice of physicians, surgeons, barbers and apothecaries, in enforcing the rules of professional conduct and in taking the necessary disciplinary measures. The medico-political functions consisted in advising the government on medical matters.

The example of Italy was followed by other nations, and various colleges of physicians were founded. The first in France were at Nimes (1397) and Bordeaux (1411). Later, colleges were founded in London (1518), Rouen (1538), Lyon (1577), Geneva (1589), Brussels (1649), Edinburgh (1689), to mention the most important. In fact a college of physicians arose in every leading town.

While colleges of physicians were founded with the object of organizing and administering medical practice, other corporations of teacher physicians and students, the Faculties, were founded with the object of teaching and conferring academic degrees. On the Continent these two groups of corporations clashed. The Faculties considered their degrees to be sufficient to allow recipients to practise medicine *urbi et orbi*. They therefore resented the exclusion of Faculty members from practice except by incorporation into the colleges on conditions imposed by those bodies. Even in the eighteenth century the Bordeaux College of physicians withheld permission from Théophile de Bordeu, a famous graduate of the Faculty of Montpellier, to practise in Pau, which came under the jurisdiction of the Bordeaux College, because he had not complied with certain collegiate conditions. All this was placing Faculties in an inferior position, and the colleges did not hesitate to interfere in University affairs. Thus when in 1749 Professor Grégoire of the Bordeaux Faculty of Medicine intrigued to nominate his son as his successor in the chair, the College of Physicians of Bordeaux intervened and insisted on a competitive examination in the interests of justice [2]. Such clashes between Colleges of Physicians and Faculties resulted in the suppression of colleges on the Continent towards the end of the eighteenth century. In Paris there has never been a college of physicians, because the Faculty of Medicine developed from early times as a very powerful body. A college of surgeons developed later and had violent struggles with the Faculty until at last it was suppressed and absorbed by its opponent.

It is my belief that this suppression influenced adversely the development of medicine in continental countries. Colleges and Faculties differ in their objects. Faculties are essentially teaching and graduating bodies, but medicine consists more in practice than in teaching. When Faculties are the sole organizers of medicine they engender dogmatism, formalism and even narrowmindedness and low ethical standards. Even from the purely scientific point of view many medical workers of originality cannot stand the academic shackles. One has only to read the history of the seventeenth and eighteenth century Faculties of Paris as depicted by Guy Patin, to grasp the truth of this adverse influence of a purely academic organization. In fact in Germany, where academic organization

reached its zenith, a powerful anti-academic movement had started in the pre-Nazi period. In France a similar movement has resulted in the recent formation of the "ordre des médecins", a sort of College of Physicians and Surgeons for the whole of France.

The College of Physicians of London (the "Royal" was affixed later) was founded in 1518 by Henry VIII at the plea of his physician, Thomas Linacre, one of the greatest figures in the history of medicine [3]. It was based on the Romano-Italian model as a corporation of physicians practising in London and a central governing and organizing body for medical matters in the London area (fixed at seven miles as periphery from the centre of the city). Government and organization were vested in the Fellows of the College, who filled vacancies in their ranks by selecting from other members of the corporation (candidates, corresponding to our contemporary members, and permissi, later called licentiates.) Similar colleges were founded later in Britain and in English-speaking countries, and colleges of surgeons developed on the same lines. In fact, contrary to its suppression on the Continent, the collegiate system endured in England and the English-speaking countries, thanks principally to the London College. Clashes between Colleges and Faculties have never been serious in this land. The most important happened in 1555, when the College of London refused to license for practice two Oxford graduates, Simon Ludford and David Laughton, on the grounds of inadequate knowledge and advised the University of Oxford to be more careful in the instruction of future physicians. After discussion with the College that University adopted a definite and more complete course of medical studies, and one of the refused candidates, the ex-Franciscan friar, Simon Ludford, underwent the better instruction, obtained his licence and was even admitted to the Fellowship [4]. On the whole the College of London, the other British colleges and the universities have worked in harmony, and many College Fellows are university teachers. The universities concentrated on their teaching functions and the colleges continued their general organizing and administrative activities in medical affairs.

As a result medical organization in England is not, as on the Continent, purely academic but collegiate-corporative, a position understood with great difficulty by our continental colleagues. In other countries the high titles in the profession are academic—such as professor, joint-professor, lecturer, and so on—whereas in England they are collegiate-corporative—Fellows of colleges, Members, &c. The difference often occasions comic episodes in international congresses, where the academic hierarchy reigning abroad allots to our Fellows a place lower even than the minor lecturers of small universities. Our colleagues abroad extricate themselves from the difficulty by giving the courtesy title of professor to every distinguished physician.

Misunderstanding of the collegiate system of medical organization is due largely to the omission or the very bare mention of the history of medical colleges in even the most complete of our treatises on the history of medicine. Historians who are not in active practice fail to understand why an institution that has disappeared from the Continent has become in English-speaking countries the most modern instrument of power for medical organization. The history of the London College is found in the works of Munk but apart from this is scattered in a multitude of papers, lectures and biographies. It can be divided conveniently according to the buildings that have housed the College, each new seat corresponding to a new century and a new line of thought and action within the College itself. It seems as if a mysterious law connects the material and the spiritual in this institution.

THE KNIGHT RIDER STREET PERIOD (1518-1614)

(THE SIXTEENTH CENTURY COLLEGE—THE COLLEGE OF LINACRE)

During this period, which corresponds roughly to the sixteenth century, the College had its seat in part of a house in Knight Rider Street. The premises belonged to Linacre, who gave them to the College, and consisted in a parlour below and a chamber above used as a council room and library. Later a capacious theatre for anatomy lectures was added and a garden secured for botanical purposes. The library was established immediately. Its nucleus was formed of books given by Linacre and, as in succeeding centuries, it was augmented by gifts, the most important being William Gilbert's bequest. In conformity with the general spirit of the College the library was from the start, as it is now, general and not purely medical.

The corporation was immediately divided into Fellows, Candidates (members) and Licentiates. As in later centuries, the activities of the College in governing and organizing

medical matters were vested in the Fellows and thus depended on their personalities. In this respect the College had a happy beginning. From the first, the original Fellows co-opted into their circle the members " the most distinguished in character and learning ", and thus the roll of the sixteenth century Fellowship includes the greatest names in the medicine of that period—Thomas Linacre, Edward Wotton, John Clement, John Caius, Sir William Butts, William Gilbert. These sixteenth century Fellows were great Greek scholars and had delved deeply into Greek thought. They had made direct contact with living Greek thinkers teaching in Italy, with Demetrios Chalcocondylis, for instance, that great philosopher and upright man, the teacher of Linacre. They had frequented the brilliant Venetian humanistic circle of Aldus Manucius, whose printing of Greek works was one of the greatest factors in the Renaissance. They were real Renaissance men of general culture and also of great character, courage and religion. No wonder that they

FIG. 3.—The Knight Rider Street College (Sixteenth Century). *Copied from " The Gold-headed Cane ".*

were capable of laying down solid foundations for our great College and for the high moral and intellectual standards that have characterized British medicine since those days.

The founders of the College laid down a triple standard for the physician as basis of their organization of medicine, a standard constituted of cultural humanistic background, free scientific thought, and high ethical qualities. The cultural humanistic background has remained an essential feature of the College. It was introduced because these first organizers of British medicine understood that medicine is not only a natural but also a cultural science. Free scientific thought, also of Greek origin, was introduced in opposition to the dogmatic scholastic thinking of the pre-College physicians. It was of

course difficult to shake off completely the authoritarianism of the Middle Ages, and we read in the Annals of the College that in 1559 John Geynes, M.D. of Oxford, had to retract his expressed opinion against the infallibility of Galen before being admitted to the Fellowship. The principle of progress, however, was there. As for the high ethical qualities, these were not the formalities of interprofessional conduct as laid down in the Florentine gild of physicians, but those high virtues of truthfulness, honesty and charity embodied in the Hippocratic teaching.

This basic triple standard was imposed by the first Fellows through their personal example—a factor powerful in the influence of the College throughout the centuries—and the various activities of the College, which can be divided into academic, administrative and medico-political.

The academic functions were teaching, examining and the award of diplomas or degrees. In those days the medical teaching given by the College was the most complete available, for the universities were not yet organized for it and their teaching of medicine was only part of general education. Anatomy lectures started in the College about 1565, the Lumleian lecture was founded in 1581, and it is probable that other non-official lectures were given. Examinations for diplomas to practise, obligatory even for university graduates, were complete and severe, and more adequate than those of the universities. Candidates were examined according to the triple standard of the College. Those who failed to attain it were rejected even if they already had a university degree, as in the cases already quoted of Simon Ludford and David Laughton. Restricted licences were granted in certain cases, as for instance to John Banister [5], a physician of great repute in Nottingham, who gave only incomplete satisfaction and notwithstanding the warm recommendation of Queen Elizabeth was allowed to practise in London only on condition that he called in consultation for difficult cases a Fellow of the College. To Thomas Fludd, a Cambridge M.D. who also failed to satisfy completely the examiners as to the adequacy of his knowledge but impressed them by his moral qualities, licence to practise was given but on condition that he should improve his knowledge by certain well-specified readings from Galen [6].

The administrative function of the College consisted first in enforcing the rule that only College graduates were allowed to practise. Thus medical practice was freed from quacks. Next, it comprised the general regulation of the conduct of physicians on the basis of the triple standard of the College. Disciplinary measures could be taken as part of administration. Richard Taylor, a Fellow, was expelled in 1590 for reprehensible conduct. Another Fellow, Walker, was summoned before the College because he had given licences to practise to several empirics from Norwich and Norfolk.

The medico-political functions of the College consisted in advising the government, the universities, various corporations and the general public on the medical aspects of education, medical organization and public health. These were important, since the College was the greatest authority in the country on medical matters. The advice given to the University of Oxford on the reform of its medical curriculum, already mentioned, was followed. Even in matters of personal appointments the government sought the advice of the College, as when Queen Elizabeth commanded the Fellows to select a member of their society to replace Dr. Henry Atkins, who after being appointed physician to the naval expedition to Spain had to be put ashore because of seasickness.

It is probable that at first the College functioned also as a learned Society, the Fellows discussing their cases and medical problems at their meetings. This function was rendered unnecessary, however, by the rise of learned societies in England during the seventeenth century. Continental writers often regard the Royal College of Physicians as an "academy of medicine", which of course is not correct.

It is unfortunate that so little is known of the sixteenth century college by the general medical public. Its great Fellows are superficially considered more as scholars than as physicians whereas in reality most of them were first-rate clinicians, as we know from contemporary testimony. The suppression of Greek from the membership diploma seems to have severed a link with their tradition. It was, however, these disciples of the Greek humanists of the Renaissance who not only laid down the foundation of the College and the high standards of British medicine but also made important contributions to the revival of medical science by reintroducing the precise scientific methods of the Greeks. Linacre paved the way for Harvey.

THE AMEN CORNER PERIOD (1614-1674)

(THE SEVENTEENTH CENTURY COLLEGE—THE COLLEGE OF HARVEY)

The Amen Corner period of the College history corresponds roughly to the seventeenth century. The Fellows moved their seat to the more spacious Amen Corner premises (at the end of Paternoster Row), which they leased from the dean and chapter of St. Paul's. A botanical garden was added, an anatomical theatre was built where Harvey taught, and the museum for housing the library was erected at the expense of Harvey. This library was greatly increased by the collection given by Harvey, and has since been called the Harveian library. Other outstanding bequests came from a German physician who admired the College, Dr. Holbosh, and from Turquet de Mayerne. When the first Harveian Librarian, Dr. Merrett, printed the first catalogue thirteen hundred volumes were listed, most of them folios rare and valuable.

During the disturbed seventeenth century the College maintained its leadership as organizer and administrator of British medicine. This was again due to the strength of its Fellowship, composed of the most famous physicians of the day. In its roll names immortal in history, such as those of Harvey, Mayerne, Glisson, Willis, Wharton and Lower are found, and with them a group of men less known but not less useful as brilliant exponents of the art of medicine, great clinicians, mostly Royal physicians. The great name of Sydenham is missing from the roll, not through jealousy or politics but because according to the by-laws the minor academic degree which was all that he had for a long time, entitled Sydenham to acceptance only as a Licentiate [7]. Later, however, the creation of honorary Fellows (1664) enabled the College to include in its Fellowship many physicians of good standing who possessed the requisite University degree but because of their age or position were unwilling to undergo the regular examinations imposed by the College. On the basis of this by-law Sir Thomas Browne, the author of *Religio Medici*, was made a Fellow. It seems remarkable that in those days of lax morals and political pressure the Fellowship maintained its high standard. There were very few disreputable characters such as Sir Alexander Frazier, a Royal physician who, if Pepys' diary is to be believed, should have been brought to trial for his notorious practices. The exceptional black sheep does not spoil the whole flock. It is to the honour of Charles II that he never exerted pressure on the College, which he admired as a learned body. The Merry Monarch may have chuckled over the witty and scurrilous attacks of one of his physicians, Gideon Harvey, on the College but he never took action, and is even said to have censured the violent attack on Thomas Willis. Only in the reign of James II was pressure made, and Fellows were expelled, notably Richard Morton, who, however, was soon afterwards reinstated. The only pressure exerted by governmental powers was the exclusion from the College of Roman Catholics, Presbyterians and Non-conformists, and to this effect the by-law allowing Fellowship exclusively to graduates of Oxford and Cambridge was enacted. The bad effects of this by-law were felt, however, only in succeeding centuries.

The academic, administrative and medico-political activities of the College continued along the lines of the sixteenth century. From the academic point of view the College retained its pre-eminence, as there was as yet no regular medical teaching in the universities. An outstanding event in the teaching of the College was Harvey's Lumleian lectures, started in 1616, in which that immortal Fellow gave the results of his research on circulation. The Goulstonian lecture was founded in 1639, the first being given by W. Rant, the second by Glisson. In those days of general scientific interest the College lectures were followed not only by physicians but by men of general culture, and Charles II himself honoured with his presence the anatomical teaching of Sir George Ent in 1665. As in academic affairs, a high standard was kept up in the administrative and medico-political spheres. The College continued as the greatest medical authority in the country. It published the first London Pharmacopœia in 1688.

The turbulent seventeenth century is reflected, however, in the life of the College. During the Civil War financial difficulties were considerable. Even the building of the College was condemned by Parliament as Church property to be sold by public auction. Dr. Baldwin Hamey, a Fellow, bought and returned it to the College In 1665, the year of the Great Plague, most of the College officers, including the custos Dr. Merrett, retired for safety to the country, and during their absence the treasure chest containing the whole fortune of the College was emptied. As a last and greatest trial came the Great Fire of 1666.

It began on a Saturday, September 1, but involved the College only on the following Wednesday. In that interval Dr. Merrett, the Harveian librarian, succeeded in removing to a place of safety many College valuables, including some hundred and forty important books, sole remnants of the Linacre, Gilbert, Harvey and Holbosh collections. After the Fire until new premises in Warwick Lane were built, the College met mostly at the house of Sir John Langham.

THE WARWICK LANE PERIOD (1674-1825)

(THE EIGHTEENTH CENTURY COLLEGE—THE COLLEGE OF THE GOLD-HEADED CANE)

The Warwick Lane period of the College history corresponds roughly to the eighteenth century. The premises in Warwick Lane were constructed especially for that purpose under the supervision of Sir Christopher Wren. It was a magnificent building worthy of the century and of the elegant "gold-headed cane" Fellows it housed. It occupied the

FIG. 4.—The Warwick Lane College (Eighteenth Century). *Copied from "The Gold-headed Cane".*

four sides of a quadrangle enclosing a spacious paved court. Its entrance from Warwick Lane was through a wide gateway closed with massive iron gates under a semicircular arch over which was a lecture theatre and a dome of curious construction, which Garth compared to a golden pill [8]. The theatre, erected at the expense of Sir John Cutler, was a model of "acoustical and optical architecture". The public rooms were spacious and handsome. The library consisted of two communicating rooms with galleries running around them. The nucleus of the library was formed of the books saved from the Knight Rider Street and Amen Corner collections by Dr. Merrett. It was rapidly enriched by gifts. The greatest of these was the magnificent collection given by the Marquess of Dorchester, more than 3,200 volumes of physics, mathematics, civil law and philology, the choicest collection of the day. Next came books bought with money left for that

purpose by Dr. Richard Hale and other gifts of Fellows, including those of Dr. Crow (Greek and Latin books), Dr. Thomas Gisborne and Dr. Baillie.

The basis of the activities of the College, its Fellowship, was not in the eighteenth century as strong and representative as in previous periods. It was less strong because, although conforming to the triple standard, the eighteenth century Fellows lacked the greatness of their predecessors. Their cultural humanistic background was more superficial and literary than deep and philosophical. Their scientific attainments were marked by the eighteenth century domination of "systems". Their moral qualities were tainted by a certain stubbornness, narrowmindedness, vanity and attachment to petty interests. The College cannot be blamed for this, as such were the features of most eighteenth century intellectuals. Even so, exceptions are met in the College itself, where Fellows like Sloane, Mead, Radcliffe, Freind, Pringle, Richard Warren and notably Heberden, the *ultimus Romanorum* of Dr. Johnson, could reach the standard of their sixteenth and seventeenth century predecessors. The Fellowship of the Warwick Lane College suffered not only from weakness but also from failure to represent all that was great in the British medicine of the day. Because of the by-law that limited the Fellowship to Oxford and Cambridge graduates, physicians so highly distinguished in character and learning as John Fothergill, William Hunter, Sir William Watson and Sir William Duncan were excluded from the Fellowship. And there was no attempt to find a way of incorporating great provincial physicians such as Erasmus Darwin, Withering, Huxham.

As the religious ban had been lifted the College justified its exclusion of all who were not graduates of the old universities by the laxity found in various foreign and even Scottish universities in the giving of degrees. There was much truth in this. The M.D. of Rheims, for example, could be obtained without residence on the basis of a thesis whose authorship was not always scrupulously investigated, and for the modest fee of four guineas. However, Scottish and foreign graduates could be incorporated into the College of London only after a very severe examination, which put them on the same intellectual level as their Oxford and Cambridge colleagues. To continue to exclude them from the Fellowship was a flagrant injustice. Disturbances occurred, some of which came before the courts. During one of these Lord Justice Mansfield, while accepting the right of the College, cautioned the Fellows against pursuing a narrow path "which might exclude even a Boerhaave" [9].

The weakness of the Fellowship during the Warwick Lane period explains the minor rôle that the College then played. The academic functions continued but the teaching was no longer superior to that of the universities, and the fairness of the examinations was marred by the kind of petty behaviour seen in the case of Isaac Schomberg. The administrative functions were maintained, but were marked by a certain obstructionism, as in the quarrel with the Society of Apothecaries and the reluctance to follow the reforms in clinical teaching advocated by Lettsom on the basis of dispensary practice. Medico-political functions, although the College was consulted in such important matters as variolization, were on the wane, for as fast as the College degenerated into an exclusive club so its authority diminished. Although, however, the College was dwindling as central organizer and administrative body in medical matters, redeeming features were the courtesy and urbanity of its Fellows, the gentlemen of the gold-headed cane. Sir William Browne, President of the College when the Licentiates, encouraged by John Fothergill among others, forced entry to the comitia, was the first to propose, although unsuccessfully, that Fothergill should be admitted to the Fellowship. The futile and petty obstruction against the Society of Apothecaries was ridiculed by a distinguished Fellow, Samuel Garth, who characterized the College of this period in this couplet:

> "Mean faction reigns where knowledge should preside
> Feuds are increased and learning laid aside."

Lettsom, an opponent of the College, was often invited to its dinners.

The weakness of the Fellowship in the eighteenth century was the more regrettable in that the life of the College underwent a crisis. Up to that time it had been the sole governing body in British medicine, the only institution possessing important academic, administrative and medico-political functions. With the eighteenth century other institutions—faculties, corporations such as that of the Apothecaries and governmental departments—took over many functions hitherto exclusive to the College. The parting of the ways was at hand. The College had either to disappear, abandoning its functions to

these other institutions, or it could maintain its leadership, but only by adapting itself to new conditions. Hence the malaise felt at the end of the Warwick Lane period.

The expression of this malaise was physical, the Fellows feeling cramped in their city abode while society and fashion moved west. The basis, however, was spiritual, and resulted from the subconscious conflict in the facing of a new situation. For a new lease of physical and spiritual life the College decided to move west, and after many efforts a site in Pall Mall East was chosen, thanks to one of its greatest presidents, Sir Henry Halford, and a new house was built for the College.

THE PALL MALL EAST PERIOD (1825—)

(THE COLLEGE OF THE NINETEENTH AND TWENTIETH CENTURIES)

The new College was opened on June 25, 1825, under the presidency of Sir Henry Halford. The magnificent ceremony, at which were present five Royal princes, most members of the government and many leading figures in national and intellectual life, symbolized the decision of the College to reaffirm its leadership.

The Fellowship was strengthened and became essentially representative of British medicine. Fellows ceased to be recruited exclusively from the ranks of Oxford and Cambridge graduates, but came from various universities. They were no longer limited to

FIG. 5.—The Pall Mall College, 1825.

London practitioners, but were chosen from all parts of Britain and the Empire. Thus the leaders of the profession were now selected in truth for distinction in character and learning independently of their religious and political views. Care was exercised to secure as Fellows men of great influence in other medical institutions, universities, hospitals, government departments and the medical section of the Services. This ensured collaboration between all factors of medical progress and contributed to the integrative function of the College in medicine. Even the most prominent Fellows of that time cannot be listed here, as all the many great names in British medicine are included.

Strong in its Fellowship the College faced the possibility that its functions might be taken over by other corporations. The problem was solved by certain modifications of activity. First of all the College increased its membership of its own " graduates " scattered throughout the world, and as over them it had absolute administrative power its influence became

extensive. Next, although academic, administrative and medico-political functions were taken over by other institutions, those of the College could be maintained on a high level as a model to other bodies; it had shown the way in the past, and had to continue as guide. Lastly, as the College, unlike the other institutions, did not specialize in any one of these functions, it was the only body capable of correlating and integrating all functions pertaining to medicine. This was also made possible by the wide representation of the Fellowship. The London College therefore remained the great central medical organizer for Great Britain and at the same time acquired international fame and esteem. Thus academic, administrative and medico-political activities of the College continued during this period on the lines of the preceding centuries. They were even intensified in order to serve as pattern.

Lectures, more extensively read than attended, often gave the last word in medical problems. The examinations maintained their high quality. For this reason hospitals required College diplomas for staff appointments, and the membership diploma impressed so deeply the powerful dean of the Paris Faculty of Medicine, Professor Bouchard, that he wished to introduce it into France as "diploma of superior medical studies". His efforts were foiled by disturbances created by students and practitioners in Paris, who were so rowdy that the police had to intervene and the Faculty buildings were occupied by the military.

The administrative functions of the College were limited to its own Licentiates, Members and Fellows, but these were now found in all parts of the globe. The medico-political functions suffered certain vicissitudes. At the beginning of the Pall Mall East period, thanks to the great personal authority of President Sir Henry Halford, the College was consulted on all important matters by the government. Later this advice was sought more rarely, and the College was running the risk of becoming a purely administrative body for its own Members and Licentiates. However, with its later presidents the College once more asserted itself and expressed opinions on medical matters of all sorts—medical education, medical organization and public health measures.

In all its activities the College maintained the triple standard laid down by the sixteenth century Fellows, and particularly the cultural humanistic background for physicians which was endangered during the ultra-positivistic and mechanistic nineteenth century. The development of this humanistic background took the form of an intensified cultivation of history of medicine, a great feature of the Pall Mall East College. History—not the collection of facts which goes by that name, but the approach to human and medical problems by means of historical philosophical thinking—is in fact the modern expression of humanistic culture. In the College itself, not only through the official history lectures (the Fitzpatrick lectures founded in 1902) but in all Harveian orations, conversazione and examinations, history of medicine was studied intensively. Knowledge of history seems to be characteristic of the modern Fellow, just as proficiency in Greek and Latin characterized the Fellows of the previous centuries. These humanistic tendencies of the College have caused not only much trembling in candidates for membership but also much head-shaking among physicians, who often believed that through this the College was "behind the times". Justification of the attitude of the College, however, is afforded by the contemporary general revival of humanistic tendencies and in the recent address of Alan Gregg [10], essentially a scientist, to the New York Academy of Medicine, in which he demonstrates the necessity of humanism in present-day medical practice.

A NEW PERIOD?

The Royal College of Physicians of London, *primum inter pares* has maintained throughout the centuries the collegiate system of organization of medical thought and practice by which all medical activities are correlated and integrated under the leadership of those who have reached the greatest proficiency in medicine. It is opposed to the academic and association systems of medical organization.

The academic system, on the wane even on the Continent where it had developed most extensively, offers direction of medical activities by the most prominent teachers incorporated in the Faculties. Faculties are specialized teaching bodies and cannot effect such complete correlation and integration of medical activities as colleges, whose foundation is wider and representation more extensive. Opposition between these two systems of medical government was evident long ago in England and ended in a *modus vivendi* by which the Faculties limited their authority to their special educational functions, the

Colleges maintaining the more general and centralizing direction of medical thought and practice.

The association system of medical organization developed mainly in the late nineteenth century, and consists in direction of medical activities under the leadership of physicians elected by universal vote of their colleagues on the basis of political and organizing capacities, independently of any proficiency in medicine. Opposition between this system and the collegiate system is developing in our own time, and again the Royal College of London is entering the lists actively. Is medical practice to be directed by leaders of majorities or by leaders in medical science and art?

This is the problem constituting the contemporary crisis of the Royal College of Physicians of London, the essential representative of the collegiate system in medicine. As happened with the rights of the Faculties, a *modus vivendi* will probably be found. Associations, such as the British Medical Association, have undoubtedly rendered and are rendering great services to medicine, but history teaches that science and art cannot be organized on a majority principle. The College which, endowed with such great will to power, has guided British medicine to the heights cannot fade away. Historical thinking, the only mode of thinking that directs action, indicates that the College will maintain its centralizing and integrating functions, the Associations of to-day like the Faculties of old keeping for themselves certain branches of medical organization. The solution will be collaboration, not opposition.

The finding of this *modus vivendi*, the solution of this new crisis, dominate the activities of the College to-day. As in the entire course of its history, spiritual fermentation in the College is bound up with the physical need for change, for moving the seat of the institution. It is at this turning-point that the bombs of the Huns attempted the destruction of the College. The building has been damaged, but the spirit, far from being subdued by the barbaric insult, has acquired an added stimulus to its work in the organization of that most civilizing of human activities, the art of Medicine.

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Section of Radiology

President—M. H. Jupe, D.M.R.E.

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Tuberculosis of the Knee-joint

By F. Campbell Golding, M.B., D.M.R.E.

Résumé.—Analyse radiologique de 100 cas de tuberculose du genou, avec le but d'évaluer l'importance et la fréquence relative des signes caractéristiques sur lesquels est basé le diagnostic radiologique.

Il n'y a eu aucune sélection des cas. Les radiographies sont les 100 premières rassemblées par le radiographe dans son département. Tous les âges entre 11 mois et 70 ans sont représentés, ce qui donne un bon tableau de ce type d'infection.

L'analyse a été faite au moyen d'une table, dans laquelle se trouvent les différents signes radiologiques typiques de la tuberculose articulaire. Les clichés furent examinés, et la présence ou l'absence de chaque signe marquée dans la table. Grâce au fait que les clichés faits au Royal National Orthopædic Hospital ont été préservés pendant de longues années, ils représentent, dans la plupart des cas, le cours de la maladie pendant tout le séjour du malade à l'hôpital.

Les signes inclus dans la table sont:

(1) Décalcification osseuse.
(2) Agrandissement de la capsule articulaire.
(3) Abcès en dehors de la capsule.
(4) Agrandissement des épiphyses et de la rotule.
(5) Rétrécissement de l'espace articulaire.
(6) Rétrécissement du cortex et élargissement de la moëlle dans la diaphyse.

Erosion:
(7) Erosion d'une moitié de la surface condylaire.
(8) Erosion des deux moitiés de la surface condylaire.
(9) Erosion de la surface articulaire de la rotule.

(10) Trabéculation grossière des extrémités des os.

Déplacement:
(11) Subluxation postérieure du tibia.
(12) Genu valgum.
(13) Genu varum.
(14) Hyperextension.

(15) Foyer primaire dans la rotule.
(16) Foyer unique bien défini dans l'épiphyse.

(17) Foyer bien défini dans la région métaphysaire.
(18) Ankylose osseuse obtenue par un traitement conservateur.
(19) Ankylose osseuse obtenue par un traitement chirurgical.
(20) Récidive après excision.
(21) Présence d'une périostéite.
(22) Infection secondaire (par sinus).
(23) Signes d'une telle infection secondaire visibles sur le cliché.
(24) Séquestre.

RESUMEN.—Intentóse un examen radiológico de 100 casos de tuberculosis de la rodilla. Su designio era de medir la importancia y frecuencia relativa de los carácteres sobre que se basa un diagnóstico radiológico.

No se hizo selección alguna de enfermos. Tomaronse las cien primeras radiografías recogidas en el departamiento por el radiólogo. Cada período de la vida se incluye desde 11 meses hasta 70 años, y así está presentado un verdadero corte transversal de este tipo de infección.

El examen se efectuó por medio de un cuadro en que eran inscritos los rasgos radiográficos típicos. Pues examinóse los films y registróse la presencia o ausencia de características particulares. En su mayor parte los films indicaban el curso de la enfermedad desde la primera hospitalización hasta la salida final tras el tratamiento. Eso lo hizo posible el que se ha conservado los films radiológicos en el Royal National Orthopædic Hospital por más de 20 años.

Las características que se incluyeron en el cuadro eran:

(1) Decalcificación del hueso.
(2) Agrandamiento de la cápsula articular.
(3) Presencia de absceso fuera de la cápsula.
(4) Agrandamiento de epífisis y rótula.
(5) Reducción del espacio articular.
(6) Reducción de la corteza del fuste y ensanche de la médula.
Erosión: (7) Presencia de erosión de una mitad de la superficie cóndilar.
Erosión: (8) Presencia de erosión de las dos superficies cóndilares.
Erosión: (9) Presencia de erosión de la superficie articular de la rótula.
(10) Trabeculación gruesa de las extremidades de huesos.
Desplazamiento: (11) Subluxación posterior de la tibia.
Desplazamiento: (12) Genu valgum.
Desplazamiento: (13) Genu varum.
Desplazamiento: (14) Hiperextensión.
(15) Foco primario en la rótula.
(16) Presencia de foco único bien demarcado en las epífisis.
(17) Presencia de foco bien demarcado cerca de las metáfisis.
(18) Anquilosis de hueso siguiendo tratamiento conservativo.
(19) Anquilosis de hueso siguiendo tratamiento operatorio.
(20) Reaparición tras excisión.
(21) Presencia de periostitis.
(22) Presencia de infección secundaria (por seno).
(23) Evidencia sobre el film de esta infección secundaria.
(24) Secuestro.

RESUMO.—Deligenciou-se fazer um exame radiologico de 100 casos de tuberculose da articulação do joelho. Este exame teve por fim descobrir a importancia e a frequencia relativa dos caracteristicos em que se baseia um diagnostico radiologico.

Não se fez seleção de doentes. Tiraram-se radiografias dos primeiros cem que appareceram na respectiva secção. Neste numero estão incluidos grupos de todas as edades, desde os 11 meses aos 70 anos de idade, podendo-se portanto fazer uma verdadeira idea deste tipo de infeção.

O metodo adotado para fazer este exame foi o de se fazer um mapa onde foram indicados todos os caracteristicos tipicos de uma articulação tuberculosa revelados pelos

raios X; as peliculas foram examinadas e registou-se a presença ou auzencia de caracteristicos individuaes. Na maioria dos casos, as peliculas mostravam a historia do curso da doença, desde a entrada do doente, até á sua saida eventual, depois do tratamento. Poude fazer-se isto pela razão das peliculas terem sido guardadas no Royal National Orthopaedic Hospital por mais de 20 anos.

Os caracteristicos indicados no mapa foram:

(1) Descalcificação do osso.
(2) Dilatação da capsula da articulação.
(3) Presença de abcesso fóra da capsula.
(4) Dilatação da epifisis e da rotula.
(5) Contração do espaço da articulação.
(6) Contração do cortex do eixo e dilatação da medula.
Corrosão: (7) Presença de corrosão de metado da superficie condilar.
Corrosão: (8) Presença de corrosão de ambas as superficies condilares.
Corrosão: (9) Presença de corrosão da superficie articular da rotula.
(10) Trabeculação aspera das extremidades dos ossos.
Deslocamento: (11) Subluxação posterior da tibia.
Deslocamento: (12) Genu valgum.
Deslocamento: (13) Genu varum.
Deslocamento: (14) Hiperextenção.
(15) Foco primario na rotula.
(16) Presença de focos isolados claramente definidos na epifises.
(17) Presença de focos claramente definidos na região do metafises.
(18) Anquilose do osso resultado do tratamento de conservação.
(19) Anquilose do osso resultado do tratamento operatorio.
(20) Recurrencia depois da excisão.
(21) Presença de periostite.
(22) Presença de infeção secundaria (por sinus).
(23) Evidencia na pelicula desta infeção secundaria.
(24) Sequestrum.

A RADIOLOGICAL survey has been attempted of tuberculosis of the knee-joint. The number of patients has been restricted to one hundred. It was only practicable to analyse these cases in detail if the number was limited to some extent. There has been no selection of patients, they represent all age-groups from 11 months to 70 years and it is believed that the information obtained represents a true cross-section of infection of this type.

The material has been obtained in greater part from the patients who have attended the Royal National Orthopædic Hospital, London. It has been the practice of the Medical Committee of this hospital to keep X-ray films for more than twenty years and it has therefore been possible to record the earliest evidence of disease and the final result in many patients. It has happened that some patients did not attend until the disease was well advanced, but with some exceptions the course of the infection has been followed and a radiographic history obtained. This has been possible by virtue of the careful record kept by Professor Seddon, who was at this time in charge of the country branch of the hospital at Stanmore, Middlesex.

The object of the examination has been to attempt to assess the relative importance and frequency of the features on which a radiological diagnosis is based, and also possibly to correct impressions of the value of certain signs which one accepts without question or without critical analysis.

The method of the examination has been by means of a chart on which the typical X-ray features of a tuberculous joint were tabulated; the films were then examined and the presence or absence of individual features recorded.

The features included on the chart were:

(1) Decalcification of the bone.
(2) Enlargement of joint capsule.
(3) Presence of abscess outside capsule.

(4) Enlargement of epiphyses and patella.
(5) Narrowing of joint space.
(6) Narrowing of cortex of shaft and widening of medulla.
Erosion: (7) Presence of erosion of one-half of the condylar surface.
Erosion: (8) Presence of erosion of both condylar surfaces.
Erosion: (9) Presence of erosion of articular surface of patella.
(10) Coarse trabeculation of ends of bones.
Displacement: (11) Posterior subluxation of tibia.
Displacement: (12) Genu valgum.
Displacement: (13) Genu varum.
Displacement: (14) Hyperextension.
(15) Primary focus in patella.
(16) Presence of clearly defined single focus in epiphyses.
(17) Presence of clearly defined focus in region of metaphyses.
(18) Bone ankylosis as result of conservative treatment.
(19) Bone ankylosis as result of operative treatment.
(20) Recurrence after excision.
(21) Presence of periostitis.
(22) Presence of secondary infection (by sinus).
(23) Evidence on film of this secondary infection.
(24) Sequestrum.

Local osteoporosis of the bones of the joint is an almost constant finding in tuberculosis of the knee. It was present in 82% of the patients who were examined. Of the remainder 8% were not seen at the hospital in the early stages and 3% died from miliary tuberculosis before there was definite evidence of radiographic change in the joints apart from capsular distension. In 7% of the patients osteoporosis was absent.

The osteoporosis develops a few months *after* clinical signs are manifest. It is often absent when the patient first attends in the Out-patient Department. The time of appearance and depth of osteoporosis depend on the severity of the onset; the latter may vary greatly. Several patients suffered from tuberculosis of the knee for long periods before erosion of the bones was evident. This period was more than three years in some instances. During this time osteoporosis was often present with little variation in degree (fig. 1).

The osteoporosis usually extends to a depth of about four or more inches in either bone and fades into the normal structure. This type of osteoporosis has certain characteristic features. The distribution is homogeneous in the affected part and is not the "spotted" decalcification associated with disuse or Sudeck's atrophy (although there were 3% patients with this type of change (*see* fig. 2)). The distribution of the osteoporosis also differs from that of senility, in the latter all the bones are affected to a uniform degree.

Another type of decalcification is sometimes found in chronic synovitis of the knee following trauma or complicating the infectious diseases which tend to resolve without bone destruction, e.g., gonorrhœa. The decalcification in these cases may be diffuse or mottled, but the cortex of the bone remains clearly defined as a white line. This definition is accentuated by a fine line of rarefaction about 2 mm. broad which lies just beneath the white line.

Local osteoporosis is present throughout the active stage of tuberculosis. During quiescence and healing the calcium content of the bones improves. The return of calcium to the cortex of the subchrondral region is a useful indication of healing of the process.

A most important feature of early tuberculosis, which will be demonstrated in good films, is an *alteration in the cancellous structure* over the whole of the osteoporotic zones. The cancellous bone of the affected limb is less clearly defined than normal, the margins of the trabeculæ are frayed. This feature appears comparatively early and is commonly found in the active stage at the same time as the articular surfaces lose their sharp definition. This loss of detail in the bones and the osteoporosis of the part make it difficult to secure good films of a tuberculous joint; in addition the lesion is obscured by fluid in the joint and thickened synovial membrane.

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PLATE I.

FIG. 1.

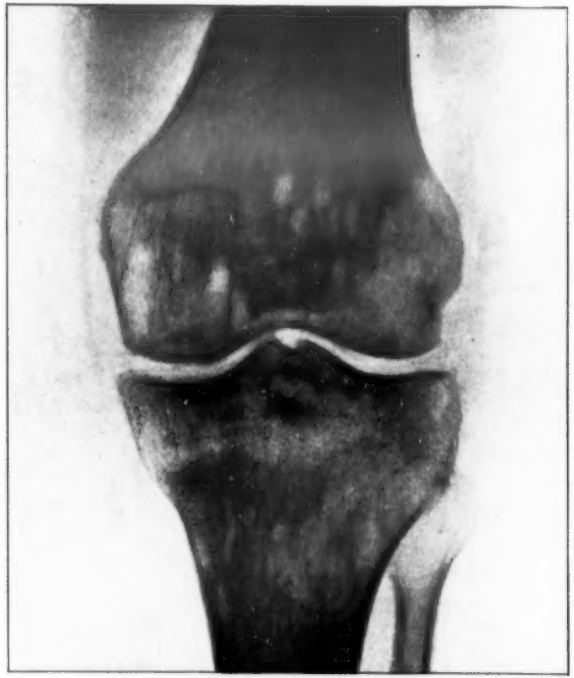

FIG. 2.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE II.

FIG. 3.

FIG. 5.

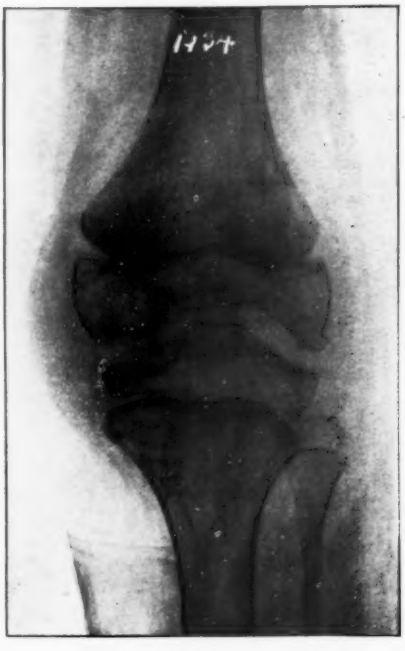

FIG. 4.

FIG. 6.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE III.

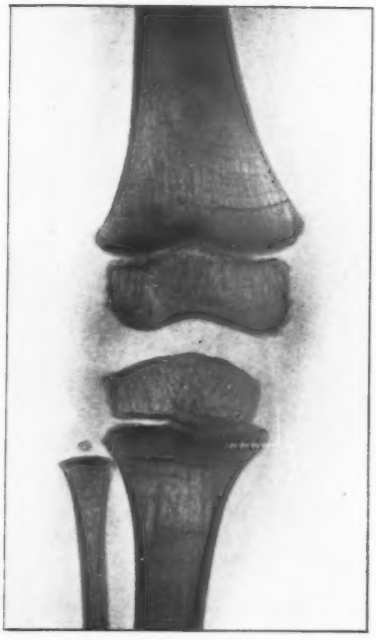

FIG. 7.

FIG. 10.

FIG. 8.

FIG. 9.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE IV.

FIG. 11.

FIG. 12.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE V.

FIG. 13.

FIG. 14.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

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PLATE VI.

FIG. 15.

FIG. 16.

FIG. 17.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE VII.

FIG. 18.

FIG. 19.

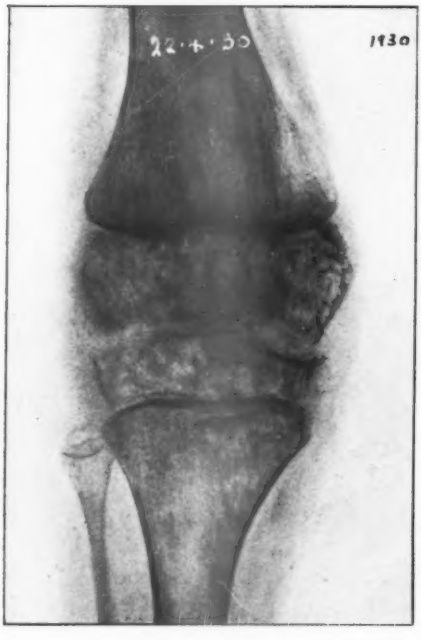

FIG. 20.

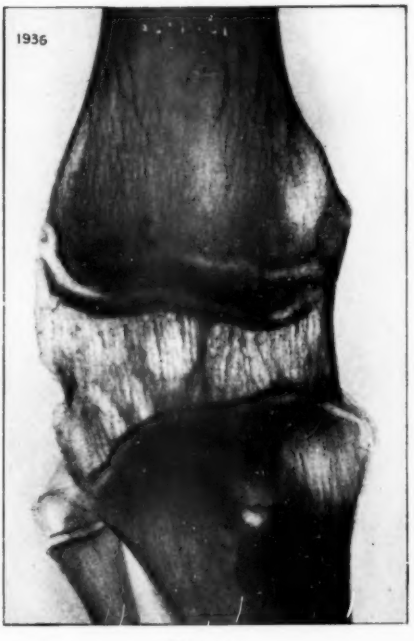

FIG. 21.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

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PLATE VIII.

FIG. 22.

FIG. 23.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE IX.

FIG. 24.

FIG. 28.

FIG. 25.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE X.

FIG. 26.

FIG. 27.

FIG. 29.

FIG. 30.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

PLATE XI.

FIG. 31.

FIG. 32.

FIG. 33.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

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PLATE XII.

FIG. 34.

FIG. 35.

FIG. 36.

F. CAMPBELL GOLDING : Tuberculosis of the Knee-joint.

A secondary effect which appears later is a *relative narrowing of the cortex of the bone and increase in width of the medulla.* This feature was present in 26% of patients. It was more marked in children than in adolescents and was very rare in adults. The oldest patient who exhibited this sign was 27 years and most of the adolescents had contracted the disease in infancy. The exact proportion which showed this alteration of structure is not reflected in this total of 26%, as patients were not included unless the change was quite definite. In order to detect the early examples comparison would have been necessary with the opposite knee and this was not part of the routine examination. Many doubtful examples were therefore omitted (*see* figs. 3, 4, 5 and 6).

A late result of continuous decalcification is an *alteration of the structure of the lamellæ of the affected region.* In many cases a progressive widening of the trabeculation was visible on the films over a number of years. The change began usually about the first to third year of infection in the moderately active disease. It was more noticeable in the child than in the adult and was present in both the synovial and osteal forms. It was particularly marked in some joints which never showed evidence of subchondral disease.

The coarse meshwork of the chronic tuberculous infection may itself simulate decalcification but the trabeculæ are thicker than normal and of average density. The wide space between trabeculæ gives a black shadow and decalcification of the whole part is simulated. This condition appears first in the epiphyses and is sometimes confined to them (*see* fig. 7), but the ends of the shafts are usually involved (*see* figs. 8 and 9). The same appearance may be noticed in the knee-joint in patients with tuberculosis of the corresponding hip.

Enlargement of the epiphyses and the patella was found in many instances. It was presumed to be a secondary result of continuous hyperæmia. The proportion showing this change was 19%. This is only a fraction of the true number as comparison with the normal limb would have been necessary to detect all cases.

The increase in size of these nuclei *was often associated with irregularity in growth;* this was most noticeable in the lateral view of the femoral condyles (*see* fig. 10). This uneven outline did not appear to be due to erosive change as the cortex was always clearly defined. The overgrowth of these parts was most noticeable in the chronic disease long before any erosion had taken place.

The stimulation of growth in this region may also affect the metaphysis. It was not uncommon to find the affected limb longer than its opposite, although this state was ultimately reversed.

Distension of the capsule of the joint was present in a large proportion of the series (71%) (*see* fig. 11). The form which is known as "caries sicca" must be a very rare type and possibly does not occur in the knee. The absence of capsular swelling in some patients was due to their attendance late in the disease.

The recognition of fluid in the joint has little value in diagnosis and apart from other signs merely serves as a signal for caution.

A soft-tissue swelling outside the joint was visible in 14% of patients. In *10% the extra-articular abscess became calcified in part.* The calcium was deposited in the wall or on the mass of the abscess. Calcification in juxta-articular abscesses is extremely rare, apart from tuberculosis.

Tuberculous abscesses tend to track in fascial planes for considerable distances. They were not, however, visible in the muscles of the thigh and calf unless some calcification had taken place. The large calcified abscesses of Pott's disease and the tuberculous hip were not a feature of this condition. The customary finding was a collection of small circumscribed deposits just above or below the joint space. They were homogeneous, dense and irregular in outline and did not exhibit any tendency to be absorbed. They frequently served as useful evidence in later years of the tuberculous origin of a joint disease. Similar calcified areas were also found in the joint. These lay in the joint or were embedded in the eroded bone near the articular end. As previously mentioned they were homogeneous and showed no evidence of bony structure. They may remain unchanged in appearance for many years (fig. 12). Two

patients with the metaphyseal type of disease showed these dense areas in the lower end of the shaft of the femur many years after the disease had healed. In each case the areas were surrounded by normal bone. It would have been extremely difficult to have made a diagnosis of their nature without the earlier films.

Narrowing of the joint space is usually associated with evidence of erosion of bone, the loss of cartilage may be more marked on one side of the joint than on the other and *it may sometimes be apparent without evidence of cortical or subcortical disease.* Early loss of cartilage space is often seen at the same time as cortical decalcification is first visible. A preliminary widening of the joint space is seldom a feature of tuberculosis of the knee, but the patella is frequently displaced forwards by synovial effusion. A unilateral widening of the joint is sometimes found; this is usually due to a combination of laxity of ligaments and a marked necrosis of the opposite condyles, producing a valgus or varus. The time of appearance of diminution of the joint space varies considerably. The organisms responsible for the acute suppurative arthritis effect, in a few weeks, a degree of cartilage loss which would be found in tuberculosis in the same number of years.

It is uncommon for the joint space to be entirely obliterated apart from bony ankylosis. Fragments of cartilage usually remain in some part and separate the ends of the bones. *Loss of cartilage was visible in 67%* of the knees examined in this series. In 15% of patients with proved tuberculosis there was no evidence of any narrowing of the joint space when the patients were discharged as healed. These included all types of tuberculous infection: synovial, osseous and metaphyseal. Of the remainder, four died before a cartilage loss might have been expected and the others are still under treatment.

(*a*) *Erosion of one-half of the condylar surfaces.*
(*b*) *Erosion of both halves of the condylar surfaces.*
(*c*) *Erosion of the patella.*

The patients considered under the heading of erosion of one-half of the condylar surfaces were those who showed evidence of superficial erosion (fig. 13). Those with a focus in the epiphysis or metaphysis above the surface were excluded. The total number who showed this type of change was 11%. It was noticed that it invariably occurred in the young patient. The oldest was only 9 years at the onset and the average age was from 3-5 years. The erosive change was seldom marked, it often extended for 5 mm. into the bone but it did not alter appreciably once it was established (fig. 14). The infection appeared to be less virulent in these patients although most of them remained under treatment for many years. Both surfaces on one side were invariably involved.

The final result was much the same as in the more generalized infection. In one instance the leg was amputated. Two patients terminated in bony ankylosis (fig. 15), and two in fibrous ankylosis. The remainder retained a degree of movement which varied from 2 degrees to 70 degrees of flexion. The condition was frequently responsible for a marked valgus or varus. This deformity differed from the type described as a lateral or medial slip of the tibia (*see* later).

An impression is probably gained by the radiologist, that almost all tuberculous knees show erosion of both condyles at some time. This feature was present in only 56% of the patients. The true figure was probably higher, as some patients left the hospital and a few died early in the disease. It is probably true that this particular type of erosion is the most characteristic feature of tuberculosis of the knee.

It is impossible to give an estimate of the time when cortical erosion will first appear. It may be months or years after the initial symptoms (figs. 16 and 17). *Once an erosion is established it shows little or no tendency to recover;* it is true that some of these areas filled in to some extent but some irregularity of the outline remained as a permanent feature. The erosive change may take the form of a dissolution of surfaces, which is more marked in the tibia than in the femur, or a localized destruction in the form of cone or thimble-shaped areas. A characteristic site for the latter is the inner tibial margin just below the joint surface (5% of the series) (fig. 18). A diffuse osteitis of both epiphyses followed cortical erosion in two patients, the whole of the cancellous structure of the epiphyses appeared to be involved (fig. 19). In both instances the disease spread through the epiphyseal lines into the metaphyses. This excursion of the process only

occurred at small points and was difficult to detect on the films. In one patient the condition was shown more clearly by the secondary infection which followed multiple sinuses, the bone of the affected region then became more sclerosed and this accentuated the limits of the diseased areas (figs. 20 and 21). Surface erosions may extend deeply into subchondral bone and sometimes assume a dentate form (fig. 22).

Apart from two patients with diffuse osteitis, a primary infection of the joint progressed to metaphyseal involvement in five others. These showed at first only the customary articular destruction. The exact depth of involvement of the bone was often difficult to determine. It was sometimes found at operation that rarefied areas on the film, which appeared to be part of the general rarefaction, represented large recesses filled with tuberculous material. Small cavities were sometimes visible as far as two inches from the articular surface without any obvious path of infection; these cavities were often identified only by small dense sequestra which they contained (3%).

Erosion of the articular surface of the patella was present in 27% of the patients, it was only a part of a more generalized disease. The patella appeared to be the primary osseous focus in only two patients. In one instance the whole bone was denser than normal and there appeared to be a diffuse osteitis (fig. 23). In the other there was a localized and clearly defined area of destruction without peripheral reaction of any kind (figs. 24 and 25).

Dislocation of the joint was not present at any time in any of this series of patients. The abnormalities, in their order of frequency, were genu valgum 28%, posterior subluxation of the tibia 20%, genu varum 8%, hyperextension 7%.

A true genu valgum was usually due to a major erosion of the lateral condylar surfaces with a local loss of the cartilage space, but the most frequent type of valgus was a lateral displacement of the whole of the shaft of the tibia at the knee-joint. Similarly genum varum was due to varus or a medial slip of the tibia.

Presence of a single focus in the epiphyses.—The number showing this feature was very small, 2% (figs. 26 and 27). The preponderance of the synovial origin of infection appeared to be overwhelming. It is not, however, always possible to distinguish between the two modes of onset in a radiograph. Some patients, not included in this small number, with an osseous focus might have been included by a different observer. It was noticed that osseous foci of this type were sometimes multiple and it was also noticed that the cartilage frequently became thin at an early stage, both of which suggested that extensive tuberculous pannus was present and there was no method by which it could be decided whether the pannus had preceded the erosion or not.

A small group of patients, 3%, showed a focus in the metaphysis, in 6% a focus had spread through the epiphysial line to involve both epiphysis and metaphysis. It was often difficult to be certain on which side of the epiphyseal line the disease had commenced. The greater area of destruction was usually in the metaphysis and the disease probably arose in this region in most of these patients. The average age of the patients with a focus in the metaphysis irrespective of its origin was 2 years 6 months, when symptoms were first noticed by the parents. The oldest patient was only 3 years. A sequestrum was visible in the cavity in three patients. These sequestra were seldom as clearly defined as in septic bone lesions.

The metaphyseal lesion is usually comparatively large when the patient is first examined. It is always found as a single focus close to or in contact with the epiphyseal line. It is usually irregularly oval and may resemble a cyst, but its demarcation from the surrounding bone is less clearly defined than in a cyst. In some parts a thin wall of sclerosed bone simulates a capsule but this is incomplete. The bone beyond this zone is unaltered. Within the rarefied area one or more sequestra may be seen. They are composed of irregular and structureless bone whose density is only slightly greater than normal (fig. 28). In some cases these sequestra may be entirely absorbed by granulation tissue. The definition of these sequestra is often so poor that they may be overlooked. The local disease seldom breaks through the cortex of the bone but usually extends towards the joint. In one patient the whole medulla at the end of the diaphysis was eroded but the cortex was intact. The epiphyseal cartilage which is so effective in blocking the spread of the septic bone disease offers no resistance to the tuberculous infection. A local expansion of the cortex is unusual and, when present, is usually slight; it is more common

in tuberculosis of the diaphysis than of the metaphysis. Periostitis over the affected area was present in a third of the patients, it varied in degree and often showed areas of destruction within it.

Bony ankylosis on conservative treatment.—It is possibly true that the orthopædic surgeon regards bony ankylosis as a comparatively rare event as the result of conservative treatment. Possibly it is also believed that bony ankylosis is more prone to occur after secondary infection from a sinus. These cases did not support either of these conclusions.

15% of patients of this series showed complete bony ankylosis on conservative treatment, of these only five had developed a sinus and presumably suffered a secondary infection. Bony ankylosis was usually complete. In some instances a trace of the joint space was left but the remainder was filled in by bone. This suggested that contact between the ends of the bones was not an essential precursor to ankylosis. The process appeared capable of filling the gaps by the formation of bone (figs. 29, 30, 31, 32 and 33).

Ankylosis after operation and operative results.—Bony ankylosis was secured by operation in 25% of the patients, of these, seven developed a sinus and showed some evidence of activity after operation. This activity subsided spontaneously or after exploration of the sinus with removal of sequestra and firm bony ankylosis was eventually obtained. In five patients excision failed and amputation had to be performed. In three instances amputation was performed without previous excision. In two patients a fibrous ankylosis was obtained by excision and re-excision had to be performed (figs. 34 and 35).

Periostitis was not very often found (18%), and was seldom extensive. It usually consisted of a single layer of periosteal bone near the joint. It was most marked in the metaphyseal form of the disease in young patients. These patients frequently showed numerous layers of periosteal bone which on close inspection were found to be irregular in places, suggesting that the disease process had extended into the periosteal bone after it had formed.

Of the eighteen patients in whom the condition was present, ten had previously developed a sinus and the periostitis was possibly due to a secondary infection in a large proportion of these patients.

The presence of one or more sinuses was recorded in the notes of 32% of patients. The sinus often remained for a very short time. Certain effects are thought to be more common in the presence of a secondary infection, amongst these are sclerosis of affected bone, periostitis, sequestra and ultimately new bone formation.

It was impossible to determine whether a secondary infection had resulted in some patients. The radiological evidence of a combined infection was frequently lacking, even in those patients whose sinus persisted for some years. In other words sclerosis of bone does not necessarily follow sinus formation.

Sequestra were visible in the end of the bone or in the joint space in 23% of the series. This figure was higher than was expected, but it included the post-operative sequestra (5%) and it should be pointed out that all the patients of the series were radiographed at intervals over a period of many years and any small sequestra, which were ultimately absorbed or removed, were probably detected. The formation of large sequestra is not a characteristic feature of tuberculosis of the knee. A large sequestrum developed in the femoral condyle of one patient in the absence of a secondary infection. No other patient showed a sequestrum which approached this dimension. This particle retained the trabeculated appearance of bone although it was more sclerosed than normal and was obviously separated from the surrounding bone (fig. 36). Most sequestra were small dense structureless particles. Sequestra were sometimes found in a small cavity in the shaft of one of the bones at some distance from the affected joint. The depth of these sequestra measured as much as two inches in some cases. It was doubtful if the extent of the disease would have been recognized, in many of these patients, in the absence of these sequestra.

FIG. 1.—The history was of four months' duration. The patient was seen in February 1937; at this time the physical findings were: "Pale pulpy swelling of knee, slightly warmer than the opposite side, synovial membrane doughy. Joint held in position of 5 degrees flexion and impossible to extend it, slight pain when the latter attempted. Several degrees limitation of flexion only. No cold abscess or sinuses, ¾ in. wasting of thigh."

In March 1937 an inguinal lymph gland was excised, this was guinea-pig positive. The patient was under treatment continually, the last note in July 1941 shows that the condition is very satisfactory with a full range of movement.

The film shows only slight osteoporosis without erosion or loss of cartilage. The disease had been present two years and three months at this time.

FIG. 2.—Disease present ten months. The patient gave birth to a child one month ago. One month after the film was taken 90 c.c. of thick yellow pus were aspirated. Guinea-pig inoculation was positive. Six months later the knee was excised. This type of mottled decalcification is rare during the early stage of infection.

FIGS. 3, 4, 5 and 6.—The patient was admitted in 1932. The history was of four months' duration. She was under treatment until August 1, 1941. She had then given up the calliper for three months. The films show a fairly typical example of the course of a tuberculous knee over a period of six years. They exemplify many of the features already described and some which follow in the subsequent paragraphs.

FIG. 3.—The disease had been present six months; only slight irregularity of the femoral condyles is visible with capsular distension. There is also slight blurring of the trabeculation of the condyles but this feature was demonstrated much more clearly by comparison with the healthy knee.

FIG. 4.—Two years later the disease had advanced considerably. All articular surfaces are eroded. The trabeculation is poorly defined and the bones are decalcified. Some fluid is present in the capsule. The width of the cortical bone is less.

FIG. 5.—Two years later. There is now evidence of quiescence. The trabeculae are more sharply outlined. Some calcium has returned. The margins of the eroded areas are comparatively smooth.

FIG. 6.—There is no evidence of activity, all the features present in fig. 5 are accentuated.

FIG. 7.—History of two years seven months' duration. An enlarged inguinal gland was removed. Section showed a tuberculous lymphadenitis. Patient is still under treatment four years after the onset wearing a moulded leather splint and condition is quiescent.

The film shows coarse trabeculation of the epiphyses without erosive change or loss of cartilage.

FIGS. 8 and 9.—The patient was under treatment for tuberculosis of the right hip. The duration of this condition was approximately seven months. The left knee then became swollen and 20 c.c. of thick slightly opaque amber fluid were aspirated. Guinea-pig inoculation was positive. An abscess formed behind the knee one year after the first film was taken, this was aspirated on several occasions. Six weeks after the first aspiration a sinus formed, this remained open for six months. In July 1939 the notes record: Left knee = no symptoms. Extension full. 80 degrees flexion.

The films show the marked alteration which may take place in cancellous structure in a proved case of tuberculosis during two years and seven months, fig. 9 is the earlier film (10.8.36 to 17.3.39). They also show that a case may terminate without loss of joint space or bony erosion, and with a large range of movement.

FIG. 10.—History of six years and five months' duration. During this time there have been periodic attacks of swelling and pain with subsidence. The patient is still under treatment. Section done six years ago showed one area of synovial membrane which indicated an early tuberculous change.

Film shows an undulating outline of the femoral condyles. There has never been evidence of erosion.

FIG. 11.—History of twelve months' duration. Found to have apical tuberculosis. Section of inguinal gland was negative. Guinea-pig inoculation negative.

The patient developed tuberculous peritonitis and died. The diagnosis of a tuberculous knee was proved.

The film shows capsular distension behind the knee and below the patella—compare with the opposite knee. The suprapatellar extension which showed very well on the

films does not reproduce in the print. Note also the very slight blurring of the cancellous bone in the affected limb compared with the normal.

FIG. 12.—The patient was aged 44 years. She had had a tuberculous knee at the age of 7 years with a local abscess five years ago.

The film shows the calcified areas which may remain indefinitely in the region of a tuberculous joint. There is also a small strip of calcification outside the joint on the medial aspect.

FIG. 13.—Treated for tuberculous knee elsewhere from age 7 to 12 years. At the end of treatment ankylosis was said to have occurred. At the time the film was taken some movement had reappeared with slight swelling and pain. This subsided and the patient was discharged after a month. Four years later there was no pain with a few degrees of movement.

The film shows an erosive lesion confined to the internal surfaces and some lipping of the outer margin of the joint with narrowing of the cartilage. The last two features are not tuberculous in origin. The tibia has moved medially.

FIG. 14.—The patient (aged 33 years) had a tuberculous knee at 9 years. At admission there was a partial fibrous ankylosis with a few degrees of movement. This movement was painful and the joint was excised five years later. There was no evidence of activity at the time of operation. During the five years that the patient was under observation the condition did not alter.

FIG. 15.—Joint fluid was aspirated at age of 2 years and gave a positive result on guinea-pig inoculation. The infection was then of nine months' duration. The patient was treated conservatively.

The film was taken six years after the onset. It shows bony ankylosis only on the internal aspect of the joint.

FIG. 16.—The disease had been present for three years ten months. Biopsy = adhesions with fine marginal pannus, cartilage slightly pitted, patella completely covered with deep red pannus. Section suggested tuberculosis.

The film shows a minimal degree of erosion of one condyle posteriorly. This was the only evidence of bony disease in spite of the comparatively long history.

FIG. 17.—The knee was held in slight flexion with spasm which any attempt at movement increased. It was tender, hot and swollen. Disease present twelve years three months. An inguinal gland was removed, " The section showed a tuberculous lesion ".

Four years after this film was taken the appearance of the condyles had not changed from that shown, but there was slight narrowing of the lateral cartilage space.

The film shows only the slightest irregularity and density of the lateral joint surfaces two and a quarter years after the onset of the disease.

FIG. 18.—The patient was under treatment for three years until evacuated in 1939, during this time some swelling of the knee persisted. Clinically it was described as typically synovial. A gland was excised in the groin; the report stated: "The section shows a tuberculous lymph gland ".

Film: the X-ray was taken two and a half years after the onset. The joint space is intact but there is some marginal irregularity particularly on the inner edge of the tibia.

FIG. 19.—Five years' history. There is evidence of a tuberculous epiphysitis with some local enlargement of the condyle. The joint space is narrowed and the tibiai articular surface is slightly affected. The condition terminated in ankylosis.

FIGS. 20 and 21.—History of three years and four months' duration. One year before the first film was taken an abscess formed and was aspirated. The aspiration had to be repeated several times. Tubercle bacilli were found on direct films. A sinus formed. A modified excision was performed in 1931. A cuneiform osteotomy was done to correct the position.

FIG. 20.—The film shows a diffuse osteitis of both epiphyses with destruction of the joint and a possible extension into the end of the shaft of the tibia on the medial side.

FIG. 21.—There is firm bony ankylosis after the arthrodesis but the disease has spread through both epiphyseal lines, beneath these lines are areas of irregular density.

FIG. 22.—History of two years eleven months' duration. The patient developed a tuberculous kidney and tuberculous sacro-iliac joint with a terminal tuberculous meningitis. The diagnosis of a tuberculous arthritis was proved.

The film, taken when the disease was still active, shows a fairly typical tuberculous arthritis of an active destructive type.

FIG. 23.—Three years' history. Patient also has had tuberculous peritonitis, tuberculous ankle and shoulder and pleural effusion. Treated in sanatorium nine months for the chest.

One year after the film was taken an excision of the knee-joint was performed. Section of tissue removed showed tuberculous inflammatory change.

The film shows some blurring and a slight increase in density of the cancellous bone of the patella and some erosion. This was the first site at which bony change was evident.

FIGS. 24 and 25.—Condition began in 1922. A sinus formed in 1926 and discharged for five months. The disease gradually healed and in 1937 extension was almost full with flexion to 30 degrees.

FIG. 24.—Film taken in September 1929. The first evidence of bony erosion occurred at the upper margin of the patella. The film shows the peculiar tendency of the tuberculous process to involve the opposing surface.

FIG. 25.—Same patient as fig. 24. The second film was taken in 1937. The lesion of the patella has healed; an area resembling a cyst marks the site of the femoral erosion. Note the undulating surface of the femoral condyles.

FIGS. 26 and 27.—The history was of eight months' duration. A Laralle operation was performed. A piece of synovial membrane was removed. This showed the presence of tuberculous granulation tissue and a guinea-pig inoculation was positive.

FIG. 26.—There is a well-defined tuberculous abscess in the internal condyle containing a sequestrum. The joint capsule is distended.

FIG. 27.—The same patient two years and six months after the operation. The clinical condition was not as satisfactory as the radiological appearance suggests. There had been intermittent discharge from sinuses and five years after the operation (September 1941) a scar on the medial side had broken down again, the range of movement was 20 degrees of flexion with extension incomplete by 10 degrees.

FIG. 28.—History of injury four years ago to knee. Tuberculosis of the joint resulted, received hospital treatment and was discharged wearing a weight-relieving calliper, it was satisfactory until there was a recurrence of pain and pyrexia; she was admitted to the Royal National Orthopædic Hospital. The abscess was evacuated. The epiphyseal line was involved. The report on the granulation tissue was " probably tubercle ". The culture remained sterile. The patient remained under observation for seven years.

Film: Shows an abscess cavity extending to the epiphyseal line and containing a sequestrum. There is no evidence of joint involvement although joint symptoms were present for four years before admission and eighteen months later, when there is a note: " Still hot and synovial thickening + +."

FIGS. 29 and 30.—Swelling of knee of about two and a half years' duration. Fluid was aspirated and was guinea-pig positive.

FIG. 29.—There is only very slight irregularity of articular bone and there is a suggestion of bone formation occurring across the cartilage space of the joint.

FIG. 30.—This is the same patient as fig. 29. The film was taken seven years later, there is firm bony ankylosis. The bone appears to have bridged the cartilage space.

FIG. 31.—The patient was first admitted at 5 years with a history of " a bad knee for a long time ", no more definite history could be obtained. There was a gross valgus deformity and backward displacement of the tibia. The knee was manipulated under anæsthesia to improve the position and was then fixed in plaster. Two years later developed a sinus, eighteen months later fibrous ankylosis is reported with ¼ in. lengthening. Six months later there was early bony fusion.

The film was taken eight years after admission. In addition to bony ankylosis it shows coarse trabeculation of the epiphyses.

FIGS. 32 and 33.—The history was of eleven months' duration. The condition was satisfactory for five years when an abscess formed in the popliteal space. Sinuses formed

and discharged for six months. Guinea-pig inoculation was positive.

FIG. 32.—The joint is distended by fluid. There is slight irregularity of the condylar surfaces.

FIG. 33.—The same patient as fig. 32, film taken six years later. Firm bony ankylosis on conservative treatment. Twelve years after the original film there had been no change from fig. 33. It appears that the disease had spread through the epiphyseal line of the tibia posteriorly but this lesion resolved.

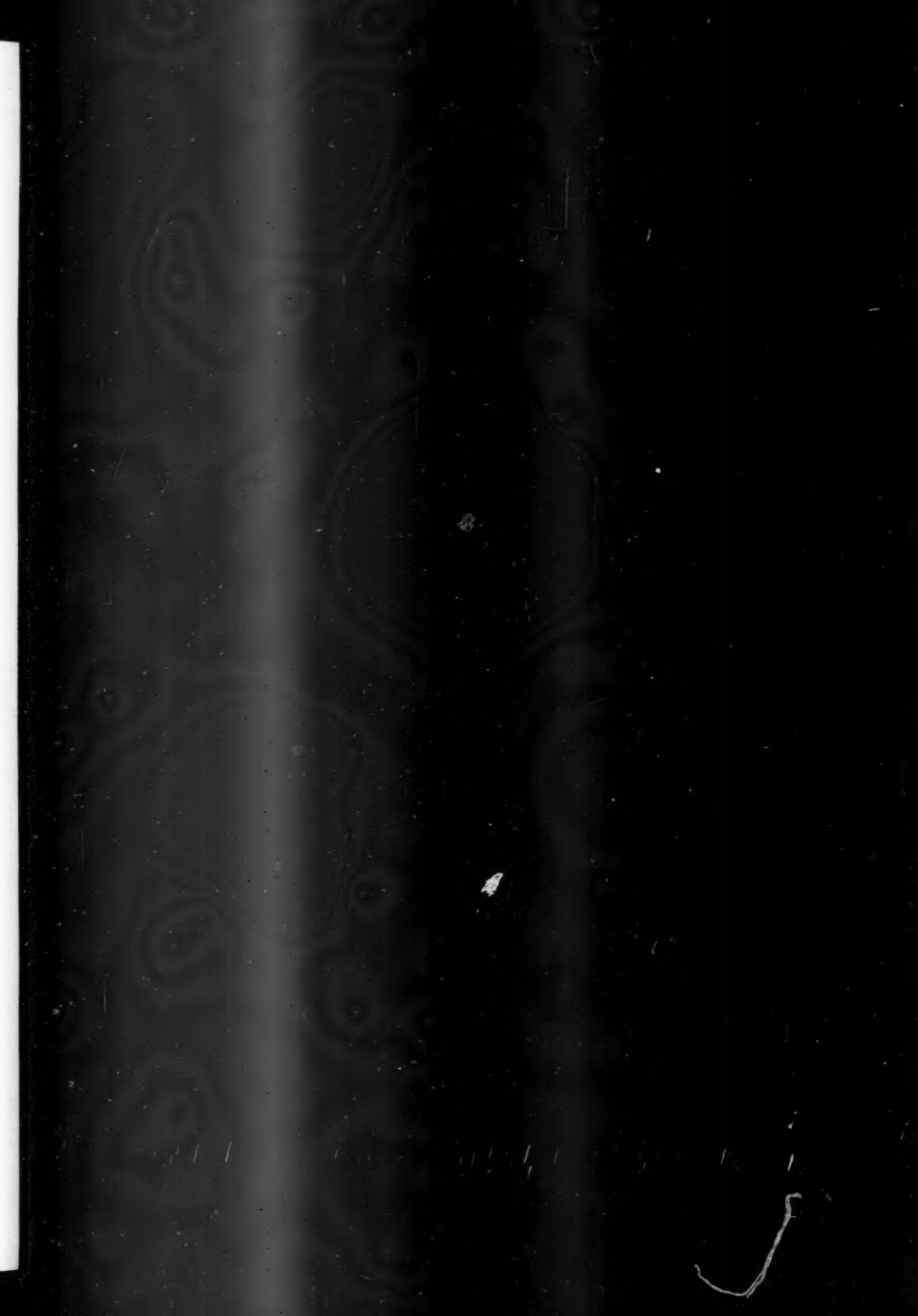
FIGS. 34 and 35.—The history was of five years' duration. Clinically the condition appeared fairly satisfactory at this time; there was no swelling or local heat, but nine months later a sinus formed, this discharged for a year. An arthrodesis was then performed.

FIG. 34.—*The film* shows only very slight irregularity of the medial joint surfaces in spite of the fact that the disease had been present for five years. It might have been thought on the X-ray evidence that the condition was not severe and would resolve.

FIG. 35.—Same patient as fig. 34 five years and eleven months after arthrodesis.

FIG. 36.—In 1921 tubercle bacilli were found in the urine. 1923 diagnosis made of tuberculosis of testicle. The patient had trouble with the knee at this time, it was swollen and was put in a splint. He had no further trouble until 1932 when the knee became painful, it was manipulated by a bone setter but became worse.

The film was taken in December 1934, an excision was performed at that time and bony ankylosis was secured. The appearances of the film are those of a very active infection with much destruction of cartilage and bone. The sequestrum is visible on the lateral side of the femur. There are also numerous small, loose fragments.



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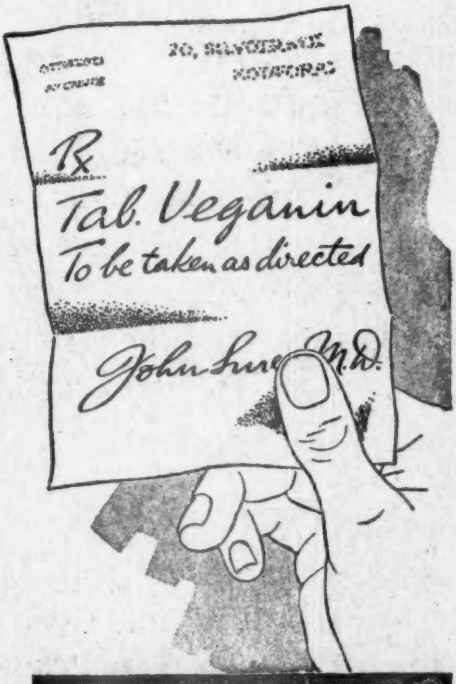

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